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MENTAL SYMPTOMS IN CASES OF SUBTENTORIAL TUMOR

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In two previous communications [1] we reported the results of our observations on the incidence and nature of mental symptoms in 85 cases of tumor involving the frontal lobe and in 110 cases of tumor involving the temporal lobe. In the present communication we report the results of a similar investigation based on the observation of patients with the tumor situated below the tentorium.

MATERIAL AND METHOD

This study was based on 120 personally observed cases, in 63 of which the diagnosis was verified by operation and in 57 by necropsy. The location of the tumors and their histologic nature are shown in the accompanying table.

We analyzed the material from the point of view of disturbances in sensorium, affect, memory and orientation, intellect and higher psychic functions, changes in personality, sphincteric control and the psychosexual sphere. Transitory or permanent abnormal mental reactions following intracranial operation or injection of air were not included in this study.

RESULTS

Mental symptoms were observed in 56 (47 per cent) of the patients with infratentorial tumor, the incidence being half that in our previously reported cases of supratentorial tumor.[1]

We have previously [1] commented on the statistical disparity encountered in the reports in the literature as to the frequency of mental

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1. Strauss, I., and Keschner, M.: Mental Symptoms in Cases of Tumor of the Frontal Lobe, Arch. Neurol. & Psychiat. **33**:986 (May) 1935. Keschner, M.; Bender, M. B., and Strauss, I.: Mental Symptoms in Cases of Tumor of the Temporal Lobe, ibid. **35**:572 (March) 1936.

symptoms in cases of tumor of the frontal and the temporal lobe. This disparity is still greater when one reviews the literature on the occurrence of mental symptoms in cases of tumor located below the tentorium. Davidoff [2] stated that psychotic manifestations other than apathy or drowsiness are unusual in association with tumor of the posterior fossa. Southerland [3] reported that in 3 (2.3 per cent) of 128 patients with verified tumor of the posterior cranial fossa, intellectual deterioration and mental impairment were recorded. Golla,[4] in a report on 22 patients suffering from tumor of the brain with mental symptoms, from the Claybury Mental Hospital, mentioned only 3 cases in which the tumor was situated below the tentorium. In another series of 33 patients with tumor of the brain and mental symptoms, from the Maudsley Hospital and allied hospitals for persons with mental disease, to which the same author referred, there were none with subtentorial tumor. In 9 patients

Location and Histologic Diagnosis of 120 Tumors Situated Below the Tentorium

Type of Tumor	Cerebellum	Cerebellopontile Angle	Brain Stem	Total
Glioma	35	2	9	46
Neurofibroma	..	23	..	23
Meningioma	3	5	4	12
Medulloblastoma	7	..	1	8
Sarcoma	7	1	..	8
Hemangioma	6	..	1	7
Metastatic carcinoma	4	..	..	4
Tuberculoma	2	..	..	2
Neuro-epithelioma	1	..	..	1
Hemangioblastoma	1	..	..	1
Cysticercus cyst	..	..	1	1
Unclassified	..	4	3	7
All types	66	35	19	120

with subtentorial tumor Minski [5] stated that mental changes were not observed until increased intracranial pressure produced apathy and somnolence and later coma. Schuster [6] observed mental symptoms in 33 per cent of patients with cerebellar tumor and in 75 per cent of patients with tumor involving the brain stem. Kraepelin [7] reported that he had repeatedly observed delusions and hallucinations in patients with tumor of the cerebellum.

The incidence of mental symptoms (47 per cent) in our series of cases of infratentorial tumor was strikingly higher than that in the

2. Davidoff, L. M.: Mental Symptoms Among Brain Tumor Patients, and Brain Tumors Among the Insane, New York State J. Med. **30**:1205 (Oct. 15) 1930.

3. Southerland, R. W.: Three Cases of Tumor in Posterior Cranial Fossa with Mental Symptoms, Bull. Neurol. Inst. New York **2**:144 (March) 1932.

4. Golla, F. L.: Discussion on the Mental Symptoms Associated with Cerebral Tumors, Proc. Roy. Soc. Med. **24**:1000, 1931.

5. Minski, L.: Mental Symptoms Associated with Fifty-Eight Cases of Cerebral Tumor, J. Neurol. & Psychopath. **13**:330 (April) 1933.

6. Schuster, P.: Psychische Störungen bei Hirntumoren, Stuttgart, Ferdinand Enke, 1902.

7. Kraepelin, E.: Psychiatrie, Leipzig, J. A. Barth, 1903-1904, pt. 2, p. 38

series of other observers. This, we believe, is due to the detailed psychiatric examination to which our patients were subjected as a routine. We found that many patients presented mental changes so slight that unless one searched for them with great care they could have escaped detection.

In 14 (12 per cent) of our series of cases of infratentorial tumor mental symptoms were among the early indications of the presence of tumor. In the following 3 cases they were the first indication of the disease:

CASE 1.—A man aged 24 was admitted to the hospital with the history that seven months prior to his admission, after the death of his mother, he became unusually irritable and unduly depressed and complained of headache. One month later he became secretive and disinterested and careless about his personal appearance. Five months before his admission he suffered from severe abdominal pain and vomited frequently. Two months before his admission there developed dizziness, buzzing in both ears, double vision and pain in the eyeballs when looking at a light. Six weeks later he became unsteady in gait and increasingly constipated and had difficulty in micturition. He lost considerable weight and became progressively worse.

Examination revealed: rigidity of the neck; a Kernig sign bilaterally; photophobia and tenderness of the eyeballs; impairment of ocular movements on extreme lateral gaze, with slow coarse nystagmus in all directions, which was more marked on looking to the right; normal fundi; supranuclear facial nerve weakness on the left; signs of involvement of the pyramidal tract on the right, and bilateral dysmetria and ataxia on performing the heel to knee test. Mental examination revealed dulness, confusion, depression, defective judgment and poor memory for recent and remote events.

Lumbar puncture yielded a clear fluid under a pressure of 120 mm. of water, with 2 cells per cubic millimeter and a total protein content of 37 mg. per hundred cubic centimeters. Caloric stimulation of the right ear produced nystagmus to the left but no vertigo or past pointing, and stimulation of the left ear gave normal responses.

Craniotomy revealed a sarcoma in the region of the right cerebellopontile angle.

As far as could be determined, this patient had not shown any mental abnormality or neurosis prior to the death of his mother. The first manifestations of the disease were the mental symptoms referable to the affect and personality, so that for months the patient was thought to be suffering from a form of neurosis which was interpreted as a reaction to the death of his mother, i. e., a reaction to a situation. Not until the appearance of symptoms of involvement of the cranial nerves was an intracranial tumor suspected. The nature of the mental symptoms on his admission to the hospital left little doubt as to their organic origin.

CASE 2.—A man aged 56 was admitted to the hospital with the history that during the last four months his family had noted a change in his personality; he became unusually irritable, and his memory was defective. About the same time there developed stiffness and pain in the back of the neck, and on several occasions he vomited. Shortly thereafter he began to have intermittent headache in the frontal region. Three weeks before his admission to the hospital he remarked that

he saw "Christmas tree tinsel." One week later there appeared diplopia and vertigo and four days later a tendency to fall backward and to the right while walking.

At the time of his admission the patient was disoriented and confused. The right pupil was larger than the left, and there was impairment of upward gaze; the corneal reflex was diminished on the right; examination of the oculi fundus revealed bilateral low grade papilledema. The tendon reflexes were hyperactive, and there was a suggestion of a Babinski sign on the right. There were also dysdiadokokinesis in the left hand and unsteadiness of gait, with a tendency to fall backward and to the right.

After examination on his admission to the hospital the patient became unconscious; the head and eyes turned to the right, and there developed twitchings of the right side of the face, followed by paresis of the facial muscles on that side and tremors of both hands.

Lumbar puncture yielded a clear fluid under increased pressure. The blood pressure was 150 systolic and 89 diastolic, and the pulse rate averaged 64 beats a minute.

During the next two weeks the patient complained of severe headache and dizziness and vomited on several occasions. During this time he was confused, somewhat irrational and sleepy and at times had lapses of memory. When free from headache he was cheerful and hopeful, had no disturbances in memory and was mentally clear. Thirty-four days after his admission the papilledema was markedly increased; the tendon reflexes were depressed, and the head became retracted. Otherwise the neurologic findings were the same as on admission.

Eight days later the patient was subjected to craniotomy. A large cystic glioma, which invaded the upper surface of the left cerebellar lobe and vermis, was removed. Necropsy revealed no lesions in the brain other than the seat of the tumor which was observed at operation.

This patient's illness began with changes in personality and disturbances in memory, which persisted for four months, when there developed signs and symptoms of an expanding intracranial lesion.

CASE 3.—A girl aged 8 years was well until August 1932, when she began to brood over the family's change of residence from a house where she had been living since birth to another part of the city and because "they didn't go to the country for a summer vacation." She repeatedly pleaded to be taken back to her original home. In September 1932 she began to vomit every morning; between the bouts of vomiting she was surly and constantly reproached the parents for changing their residence. As the day advanced she became more complacent and cheerful. The family described these changes in mood as waves of depression and elation. One month later there developed severe headache, and she became unusually irritable and moody. On Dec. 21, 1932, she was admitted to the pediatric service of the Mount Sinai Hospital, with the complaint of loss of weight and headache.

Except for some emaciation physical examination at the time of admission gave normal results.

She remained in the hospital eight days, during which she was always depressed and cried a great deal, blaming her mother and sister for her condition, which she attributed to the change in residence. She also complained of headache and vomited frequently. Psychometric examination revealed that the child was of superior intelligence.

Owing to the absence of objective signs of organic disease, the patient was thought to be suffering from psychoneurosis and was referred by the pediatricians to the clinic for psychotherapy. Two weeks after the period of observation at the hospital she met with an automobile accident, which terminated fatally. Necropsy performed in another institution revealed a medulloblastoma of the vermis.

From the onset and on her admission to the hospital this patient's illness, characterized chiefly by disturbances in affect, was thought to be psychogenic. In the present state of knowledge it is impossible to say definitely whether the mental symptoms were a reaction to a psychic trauma or were due to the tumor of the brain directly—whether the psychoneurotic manifestations were precipitated by the tumor of the cerebellum or whether they were due to a combination of all these factors. In retrospect, one may be inclined to say that the mental symptoms were due to the organic disease. This case illustrates how cautious one must be in evaluating mental symptoms and in drawing conclusions from statistical data without considering other factors that may be involved in a given case.

DISTURBANCES OF THE SENSORIUM

Disturbances of the sensorium were by far the most frequent mental symptoms observed. They were present in 41 patients (32 adults and 9 children, or in 35 per cent) and were manifested chiefly by mild and transitory apathy or dulness, a tendency to somnolence, poor cooperation and lack of attention, depending on variations in the threshold of consciousness. Hallucinations were present in 4 patients.

A man, aged 56, with a large cystic glioma in the upper surface of the left cerebellar lobe and extending into the vermis had visual hallucinations; on one occasion he saw Christmas tree tinsel (case 2).

A man, aged 43, with a spongioblastoma in the lower portion of the pons and the outer surface of the upper part of the medulla occasionally saw spots or "flickers of light" of various colors. At the time he complained of these hallucinations vision and the optic fundi were normal.

A woman, aged 28, with a glioma in the right cerebellar lobe complained of seeing sparks on closing her eyes during headache and of hearing dull thuds in both ears, louder in the right.

A man, aged 58, complained of seeing halos around lights. Necropsy revealed a tumor, the size of a tangerine, embedded in the vermis and right cerebellar lobe.

Although the literature contains reports of cases of tumor of the posterior fossa in which the patient had olfactory hallucinations, we could find no such cases in our series.

The frequent occurrence of visual hallucinations in patients with supratentorial tumor involving directly or indirectly some part of the visual centers or pathways is well known. Their occurrence, however, in patients with infratentorial tumor has not been generally appreciated.

The following cases reported in the more recent literature illustrate the not infrequent occurrence of hallucinations in cases of tumor of the posterior fossa:

Deery [8] recently reported 2 cases of tumor of the posterior cranial fossa, in 1 of which the presence of visual hallucinations led to exploration of the temporal lobe; this showed nothing abnormal, but necropsy revealed an acoustic neuroma. In the second case there were definite visual and olfactory hallucinations, with signs and symptoms of cerebellar tumor. Ventriculography definitely localized the lesion in the posterior fossa; suboccipital craniotomy disclosed a dermoid cyst in the midline of the cerebellum, removal of which was followed by disappearance of the hallucinations.

Dowman and Smith [9] reported 2 cases of cerebellar tumor with visual hallucinations. One was that of a man, aged 32, who had visual hallucinations during which he saw flowers to the right. Owing to the patient's blindness, no studies of the visual fields were possible. Operation revealed a large hemangioblastoma in the right cerebellar lobe. The other case was that of a man, aged 30, who had visual hallucinations during which he saw objects on his right. There was no hemianopia. At operation a large cyst of the left cerebellar lobe was observed.

Deery [8] suggested that the hallucinations in these cases may have been due to pushing upward of the bulging tentorium, constituting a local irritation of the occipital lobe. He expressed the belief that intracranial hypertension was not the cause of the hallucinations, unless one postulates irritation of the "higher mental centers," but that interference with the blood supply to some part of the optic pathways might conceivably be a factor. The posterior cerebral artery is so situated that it might suffer from effects of pressure. By its median and posterior lateral ganglionic branches this artery supplies blood to a large part of the optic pathways from the thalamus and temporal lobe to the occipital lobe.

It has also been suggested that visual hallucinations may be due to irritation of the optic papilla and retina by the edema, hemorrhages and circulatory disturbances in these structures, and the auditory hallucinations, to similar irritative processes in the cochlear nerve.

None of the patients in this series had complex auditory or formed visual hallucinations. Thirty-one patients complained of noises or buzzing in one or both ears. In 21 of these the tumor was situated in the region of the cerebellopontile angle, in 7 in the cerebellum and in 3 in the brain stem (extramedullary). Except for 3 patients with tumor of the cerebellum, all persons who complained of hearing noises in the ears presented objective evidence of impairment of cochlear and vestibular functions on the side of the tinnitus. The tinnitus in the 28

8. Deery, E. M.: Two Cases of Tumor of Posterior Fossa Causing Visual Hallucinations, Bull. Neurol. Inst. New York **1**:97 (Jan.) 1931.

9. Dowman, C. E., and Smith, W. A.: Localizing Diagnosis in Brain Tumor, J. A. M. A. **96**:318 (Jan. 31) 1931.

patients in whom there were evidences of a pathologic process in the ear cannot therefore be regarded as a hallucination in the sense of an abnormal mental state. In the 3 patients who showed no evidence of a pathologic process in the mechanism subserving hearing, the tinnitus may have been due to a functional disturbance in the same mechanism secondary to intracranial hypertension. Here, too, it is doubtful whether the tinnitus can be regarded as a hallucination in the sense of an abnormal mental state.

It is noteworthy that, although all the 120 patients in this series showed evidences of intracranial hypertension, only 35 patients had disturbances of the sensorium. This tends to show that in patients with tumor of the brain intracranial hypertension is not the sole cause of the changes of the sensorium. The increase in the limen of consciousness in these persons must be due to some other factor or factors, the precise nature of which is not yet known. It is not unlikely that intracranial hypertension may be merely a contributing factor in the production of apathy or drowsiness, just as it may be in the production of papilledema.

DISTURBANCES IN AFFECT

Disturbances in affect were observed in 29 patients (24 per cent), 22 of whom were adults and 7 children. The changes were slight and were not persistent. Euphoria was noted in 8 patients—7 adults and 1 child. Two adults were facetious; 2 patients were both euphoric and facetious, and 4 patients manifested mild forms of depression, chiefly in the form of hypochondriasis. Several were unusually apprehensive. Eleven showed increased irritability, 3 of whom were children who cried excessively and had tantrums of temper.

From our observations on these patients we are inclined to regard the apprehensiveness as a psychogenic reaction to the symptoms produced by the tumor and not directly to the tumor. Some of the patients were worried because they suffered from severe headache and vomiting and were physically incapacitated by the disturbances in gait and equilibrium. Others were anxious and apprehensive because of uncertainty as to the nature of the disease, the necessity of undergoing an operation and the possible outcome. The reactions of these patients were similar to those described by us in patients with tumor of the temporal lobe who suffered from aphasia and were anxious, depressed and irritable because they were unable to express themselves or to be understood. In other words, we believe that these symptoms were psychic reactions of the type frequently observed in patients suffering from any severe disease.

DISTURBANCES IN MEMORY AND ORIENTATION

Nine patients, all adults, had disturbances in memory; 4 of these were also poorly oriented, and 3 were slightly confused. The presence

of disturbances in memory and orientation in children was not recorded. This may be due to the fact that the children were not subjected to special tests for memory.

CHANGES IN PERSONALITY

For the purpose of this study we considered that a patient was suffering from change in personality when the psychic component of the psychosomatic integration was so altered that his relatives and friends described him as a "different person." Sixteen patients (13 per cent)—11 adults and 5 children—showed changes in personality. In 4 patients of the entire series such changes in personality were among the early manifestations of tumor. This low incidence is in marked contrast to the high incidence of the symptom observed in patients with tumor of the frontal or the temporal lobe (chart).

DISTURBANCES IN INTELLECT AND HIGHER PSYCHIC FUNCTIONS

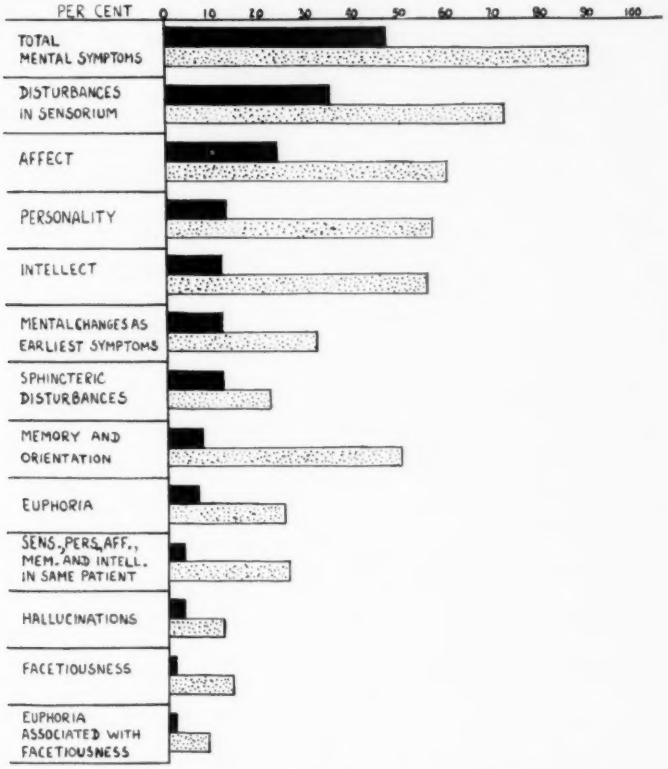
Changes in the intellect and higher psychic functions were found in 14 patients (12 per cent)—13 adults and 1 child. The disturbances in intellect were mild and were associated in all cases with disturbances of the sensorium, especially clouding of consciousness and confusion, and with other mental changes. The low incidence of this mental symptom in patients in whom the tumor was situated below the tentorium as compared with the incidence in patients with tumor above the tentorium is noteworthy.

DISTURBANCES IN SPHINCTERIC CONTROL

Fifteen patients (12 per cent)—12 adults and 3 children—had sphincteric disturbances. Five of these complained of difficulty in retaining urine and of incontinence; 2 had difficulty in starting the urinary stream; 1 had urgency of urination; 2 had urgency and inability to "hold the urine." In 2 cases the record stated that the patient had "urinary difficulty," the nature of which was not stated. One patient had incontinence of urine and feces, and 2 were recorded as "being incontinent," but it was not stated as to which sphincters were affected. In 2 cases sphincteric disturbances—difficulty in starting the urinary stream—were early manifestations of the disease; in 1 of these the tumor was in the cerebellopontile angle, and in the other there was a cysticercus cyst of the fourth ventricle. In the remaining cases sphincteric disturbance appeared relatively late in the disease.

It is noteworthy that in our series of cases of supratentorial tumor sphincteric disturbances were almost twice as frequent as in the cases of infratentorial tumor. Observations in our cases seem to confirm the

statement of Frazier, Watts and Uhle[10] that great caution must be exercised in evaluating the significance of disturbances of urination when they appear to be caused by tumors in such widely different locations as the frontal, the temporal and the occipital lobe, the diencephalon and the cerebellopontile angle. The lower incidence of such disturbances in cases of infratentorial tumor, in which the degree and incidence of intracranial hypertension were much greater than in those



Comparison of the incidence of mental symptoms in 120 cases of infratentorial tumor and in 195 cases of supratentorial tumor. The solid areas represent the incidence for infratentorial tumor, and the stippled areas, the incidence for supratentorial tumor.

of supratentorial tumor, seems to be fair evidence that intracranial hypertension in itself is not a satisfactory explanation for the occurrence of this symptom.

10. Frazier, C. H.; Watts, J. W., and Uhle, C. A. W.: Source of Visceral Impulses, A. Research Nerv. & Ment. Dis., Proc. **15**:239, 1935.

Some authors attributed the disturbances of the bladder to the mental state of the patients. While there is no doubt that mental irritability and apathy may have an effect on the tone of the bladder, as shown by the changes which Rose [11] noted in the cystometric readings in such conditions, this cannot be the entire explanation, for in several of our cases disturbances in the control of the bladder were noted even though the patient showed no abnormal mental reaction and many patients with psychic disturbances in practically every sphere had no disturbances in vesical and rectal function.

It is well known that "neurogenic bladder" may be caused by a lesion of the autonomic centers in the brain for control of the bladder. According to Brünning,[12] disturbances of the bladder of cerebral origin are of two kinds: lesions of the cortex, which produce retention of urine, and lesions of the bladder center in the thalamus, which produce incontinence of urine. The cortical center is said to be located in the region of the anterior central convolution of both cerebral hemispheres near the leg zone. By way of the pudendal nerve, these centers control the voluntary external sphincter of the bladder. From observation of wounded soldiers, both Kleist [13] and Foerster [14] placed the centers for the control of the bladder and rectum in the lower part of the paracentral lobule of the cerebrum. Kleine,[15] a pupil of Kleist, placed the bladder center on both sides of the brain in the region of the foot center and the paracentral lobule and found that symptoms of disturbance of the bladder occur only when both centers or the tracts leading to and from these centers are affected.

In their experiments on cats, Langworthy and Kolb [16] found that when the brain stem is transsected below the acoustic colliculi, micturition is abolished and the bladder shows retention of urine, with overflow.

In all probability, in our cases the symptoms of disturbance of the bladder were due to interference with the functions of the bladder center in the cortex and hypothalamus as a result of interruption of the impulses conducted by pathways from these centers as they descend

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11. Rose, D. K.: Determination of Bladder Pressure with Cystometer: A New Principle in Diagnosis, J. A. M. A. **88**:15 (Jan. 15) 1927.

12. Brünning, F.: Ueber cerebrale Blasenstörungen, Arch. f. klin. Chir. **113**: 470, 1920.

13. Kleist: Die Hirnverletzungen in ihrer Bedeutung für die Lokalisation der Hirnfunktionen, Allg. Ztschr. f. Psychiat. **74**:544, 1918.

14. Foerster, O.: Discussionsbemerkungen zum Vortrag des Kleist, Allg. Ztschr. f. Psychiat. **74**:582, 1918.

15. Kleine, W.: Ueber zerebrale Blasenstörungen, Monatschr. f. Psychiat. u. Neurol. **53**:11 (Jan.) 1923.

16. Langworthy, O. R., and Kolb, L. C.: The Encephalic Control of Tone in the Musculature of the Urinary Bladder, Brain **56**:371, 1933.

or ascend through the brain stem, because of pressure by the tumor on the brain stem.

Three patients had disturbances in the psychosexual sphere manifested by loss of the libido.

COMMENT

In our series of cases of infratentorial tumor 4 patients (all adults) showed abnormal states in all psychic spheres.

The incidence of abnormal mental states in patients with tumor of the brain situated below the tentorium was found to be half as high as that in patients in whom the tumor was located in the cerebral hemisphere. In the former group the mental symptoms were generally mild and not persistent; they appeared as a rule late in the course of the disease, and in most instances they were associated with symptoms and signs of disturbance in function of the cerebellum, brain stem and lower cranial nerves. In the group of patients with tumor in the cerebral hemisphere, the mental symptoms were more varied, severe and persistent; they frequently appeared early in the disease and were not always associated with other symptoms of tumor of the brain. It seems, therefore, that the early appearance of severe, complex and persistent abnormal mental reactions in a patient who presents no other signs and symptoms of tumor of the brain than intracranial hypertension indicates the probability that the tumor is located above rather than below the tentorium. In this sense mental symptoms may be said to have some localizing value.

The findings in our cases seem to show that when mental disturbances are the most prominent symptoms in a patient in whom the neurologic signs and symptoms point to tumor in the posterior fossa they are to be regarded as false localizing symptoms. This is illustrated in the following case.

CASE 4.—S. F., an unmarried woman aged 50, was admitted to the hospital with the chief complaint of unsteadiness in gait. Except for a nervous breakdown at the age of 43, she was in good health until two months before her admission, when she suddenly experienced attacks during which her "legs gave way." During the next five weeks these attacks became more frequent and more severe, and there developed nausea, anorexia and loss of weight. A day before admission, she became dizzy and had transient disturbances in memory.

Except for slight flattening of the lower part of the face on the right and a somewhat unsteady and cautious gait, neurologic examination gave negative results. Lumbar puncture revealed a clear, colorless fluid, under a pressure of 140 mm. of water.

While the patient was under observation, there developed slow cerebration, akinesia and progressive mental deterioration and hebetude. She also complained of nausea and headache in the frontal region, occasionally followed by vomiting. The caloric tests gave normal responses in both ears. Encephalography on two occasions revealed no air in the ventricles.

Five weeks after her admission the patient became drowsy, and incipient papilledema developed. A ventriculogram at this time revealed symmetrical internal hydrocephalus, with a dilated but tortuous iter. Suboccipital craniotomy disclosed a neurospongioblastoma which involved the left cerebellar lobe.

The almost complete absence of neurologic signs of focal cerebral disease and the presence of a mental symptom complex indicating cerebral disease led at first to a diagnosis either of degenerative disease of the brain, in the nature of Alzheimer's disease, or of tumor of the frontal lobe. The failure of air to enter the ventricles during encephalography on two occasions, however, suggested the possibility of a lesion in the posterior fossa, even though there were no definite signs of cerebellar involvement and no high degree of papilledema. The patient was therefore subjected to ventriculography, which left no doubt that the lesion was in the posterior fossa, where it was observed at operation. In this case the mental picture was a false localizing symptom.

Case 5.—S. S., a man aged 58, was admitted to the hospital on Oct. 19, 1926, with the history that five years before his admission he had had attacks of fainting which were attributed to disease of the coronary arteries. He remained well until six months prior to his admission, when there developed weakness of both lower extremities, intention tremor in both hands, emotional instability and impairment of memory. One month later he complained of seeing halos around lights and became drowsy. The weakness of the lower extremities gradually progressed, and the tremor increased. One month prior to admission diplopia developed, and one week before he was admitted to the hospital he had retention of urine, with some incontinence. He had no headache, vertigo or convulsions.

The significant findings at the time of the patient's admission were: peripheral arteriosclerosis, with a blood pressure of 140 systolic and 80 diastolic and the pulse rate varying between 80 and 94 a minute; ataxic gait and station, with a tendency to fall to the right and backward; bilateral dysdiadokokinesis and intention tremor; beginning papilledema in the right eye and 1.5 diopters of swelling in the left; weakness of the facial muscles on the right and perioral tremor; impairment of hearing on the left; guttural speech, and diminished vibration in the lower extremity on the left.

Mental examination revealed: poor cooperation, restlessness, confusion, disorientation, poor memory for past and recent events and emotional instability, associated occasionally with euphoria and facetiousness.

Lumbar puncture yielded a clear, colorless fluid under slightly increased pressure, containing 9 cells per cubic millimeter.

Three days after admission there appeared in addition to the preceding neurologic signs parkinsonian facies, mild hemiparesis on the right side, hypokinesis and incontinence of urine. An encephalogram was interpreted as indicating the probable presence of a mass in the left lateral ventricle which pressed on the third ventricle. During the next three weeks the mental condition gradually became worse, with progressive mental deterioration; at times the patient showed evidences of visual and auditory hallucinations.

One month after admission exploratory craniotomy of the left temporal lobe revealed no tumor. Twenty-five days later a ventriculogram showed marked bilateral internal hydrocephalus, with incomplete filling of the left lateral horn. Two days later Bárány tests gave normal responses on both sides. On December 17, sixty-two days after his admission to the hospital, the patient was subjected to suboccipital decompression. The surgeon reported that he encountered firm resistance within the substance of the cerebellum at a depth of 3 or 4 cm. Death occurred five days later. Necropsy revealed a meningioma, the size of a tangerine, embedded in the vermis and the right cerebellar lobe.

In this case the mental picture, associated with hallucinations, was thought to indicate a supratentorial tumor.

In our series there was apparently no significant difference in the incidence, nature and severity of the mental symptoms or in the nature of the tumor in cases in which the tumor involved the cerebellum proper (group A), the cerebellopontile angle (group B) or the brain stem (group C).

Of the patients with tumor of the cerebellum proper, 30 were under the age of 14 years, of whom 9 (30 per cent) showed abnormal states. Disturbances of the sensorium were present in 5 patients and of affect in 4 (of whom 1 was euphoric); changes in personality appeared in 4 patients and sphincteric disturbances in 3. Of the 36 adult patients in this group, 20 (55 per cent) exhibited mental symptoms, 18 disturbances of the sensorium, 10 changes in affect (4 of whom were euphoric), 7 defective memory and orientation, 5 changes in personality, 7 disturbances in intellect and higher psychic functions, 5 sphincteric disturbances and 3 changes referable to all psychic spheres. The incidence of psychic disturbances in children was 25 per cent lower than that in adults. In adults mental symptoms were more complex than in children. This is not surprising when one takes into consideration that the psychic faculties in the adult are better developed and more organized than in the child, so that even the slightest disturbance in the psychic integration is more readily detected. Furthermore, the determination of the presence or absence of disturbances in such mental faculties as intellect or memory and orientation in children is much more difficult and requires a special technic, which cannot always be employed, particularly when the child is suffering from severe headache, vertigo and vomiting. This applies especially to children under 5 years of age, whose psychic reactions and behavior are difficult to evaluate by psychometric tests and necessitate a much longer period of careful observation than can ordinarily be given to the average patient suspected of having a tumor of the brain. It is not unlikely, therefore, that the incidence of disturbances in intellect and memory and orientation is actually much higher in children than our figures seem to indicate.

Of the 35 patients (all adults) with tumor in the region of the cerebellopontile angle, 16 (46 per cent) had mental changes. Ten patients had disturbances in sensorium in the form of mental dulness or apathy; 8 had disturbances in affect, 1 of whom was euphoric and another euphoric, facetious and hypomanic; 4 were unusually irritable and 2 were mildly depressed. Seven patients had obvious changes in personality; 6 showed disturbances in intellect and higher psychic functions; 2 had defective memory; 5 had difficulties in sphincteric control, and 1, whose first symptom was depression and change in personality, had mental symptoms referable to all psychic spheres.

Of the 19 patients with tumor of the brain stem 12 were adults and 7 children. Mental symptoms were present in 7 adults and 4 children. Disturbances in sensorium were present in 11 patients (6 adults and 5 children); they were severe and characterized by marked apathy, drowsiness and torpidity; 1 patient was almost constantly in a semistuporous state. Six patients had disturbances in affect; of these, 3 were children who were hyperirritable, lacrimose and depressed, and 2 were adults who were euphoric.

Evidences of intracranial hypertension were present in almost all the patients in this series. Except perhaps for disturbances of the sensorium, which were more severe in patients with marked intracranial hypertension, there was no significant relationship between the degree of intracranial hypertension and the occurrence, nature and severity of the mental symptoms. The lower incidence of mental symptoms, as well as their relative mildness, in patients with infratentorial tumor is striking when compared with that in patients with supratentorial tumor. This is not surprising when one takes into consideration that the anatomic structures below the tentorium (cerebellum, pons, medulla and the cranial nerves) play, comparatively speaking, a minor rôle in the higher psychic functions. Whereas the cerebrum with its cortex and rich association network determines the more complex psychic processes, such as perception, memory and orientation, ideation and judgment, the chief function of the structures below the tentorium relates to the control of the finer regulation and coordination of motility and postural adjustments, as well as to the control of visceral activity (respiration, cardiac action, deglutition, digestion and phonation) and, to some extent, of vision and hearing.

SUMMARY AND CONCLUSIONS

Mental symptoms were observed in 56 (47 per cent) of 120 patients with tumor below the tentorium; they were an early manifestation of tumor in 14 patients (12 per cent) and the first symptom in 3 patients (2.5 per cent).

There was no significant difference in the incidence, nature and severity of the mental symptoms in adults as regards the nature and location of the tumor.

The mental symptoms were milder and less complex in children than in adults; this may have been due to the greater technical difficulty in eliciting slight disturbances in affect, memory and orientation and intellect in children.

Mental symptoms in cases of subtentorial tumor were much milder and less complex than those in cases of supratentorial tumor.

Crude visual hallucinations of the type usually observed in cases of supratentorial tumor may occur in cases of infratentorial tumor. They were present in 4 patients in our series.

The early appearance of profound and complex mental changes, especially those involving disturbances of memory and intellect in a patient whose only evidence of tumor of the brain is intracranial hypertension, is in favor of localization of the tumor above the tentorium; in this sense the mental picture in a patient suspected of having tumor of the brain may perhaps be of some localizing value. Too much reliance, however, is not to be placed on the mental picture for this differentiation. If studies with the use of air are indicated in a patient with such a condition, especially if the intracranial pressure is greatly increased, it is safer to resort to ventriculography than to encephalography by the lumbar route.

DISCUSSION

DR. PAUL SCHILDER, New York: This study gives valuable information and confirms one's general impression. I have no statistics at hand, but in the psychiatric service of the Bellevue Hospital, my colleagues and I rarely encounter a subtentorial tumor, whereas the incidence of tumor of the frontal lobe and of the temporal lobe is rather high. I remember only 1 patient with a cerebellar tumor who came to our service in the last few years. The mental symptoms were outspoken. Occasionally, one sees a patient with a pontile tumor with rather outspoken mental signs which in large measure remind one of moria, but on the whole the statistics given by Dr. Keschner are valuable and are decided aids for diagnostic purposes. If one tries to evaluate these data from a more psychologic point of view one would like to ask: Should it not be possible to describe psychiatric and psychologic symptoms more from the point of view of whether the personality of the patients has changed and how it has changed in consequence of the presence of tumor of the brain in different localizations? It sounds rather artificial when, in such a discussion, intellect, memory and state of consciousness are treated as separate entities. This may be necessary from the point of view of statistics, but it does not help in an understanding of what is actually going on in the patient who suffers, who has headaches and who has difficulties in getting in touch with the outside world and also in orienting himself as to what is going on inside himself.

There is need of studies on tumor of the brain in different localizations which will show in which way the total attitudes of persons change with such tumor,

and whether this change in the total attitudes differs with different localizations of the tumor. My preliminary impression is that the changes are very great, and I do think that the patient with a tumor of the cerebellum is different from a patient who is afflicted with a tumor of the frontal lobe or of the temporal lobe. The attitude toward life of the one who has a tumor of the frontal lobe is changed and his attitude toward symptoms is different from that of a patient with a tumor in a different location.

I have read in the interesting paper of Dr. Keschner about those of his patients in whom a severe reaction toward the life situation was the first symptom which came into the foreground of the clinical picture. These persons have had a psychic trauma. In the clinical picture the psychic reaction and the physical suffering blend into a unit.

One should also ask: What is the reaction of a person at the beginning of his organic disease and what is his reaction when the disease is fully developed? One sees in almost all patients with organic disease, even those in whom the organic changes is not fully developed, an accentuation of the problems of the personality. One cannot separate the personality from the clinical picture.

It is an interesting problem to decide what part the hallucinations play. The complete paper, which I read, has much more and very interesting material in this respect. I should like to draw attention to the fact that every severe impairment of the vestibular function changes the function of the consciousness, and I think some of the optical hallucinations reported are in rather close relation to vestibular disturbances.

Finally, one should not forget that every function of the body has a definite psychologic meaning. The cerebellum has to do with functions of equilibrium. This function is not merely organic; it is also psychologic. My final conclusion is: It would be important to supplement this interesting study by a study of patients with tumor of the brain, considering these patients as human beings, and to study them in the way one studies the patient with a neurosis or a so-called functional psychosis. We may then get access to interesting psychologic problems, because this material has never been used fully from a psychologic point of view. I think the study presented is a very valuable beginning, and I think those interested should go on in this work.

Dr. Israel Strauss, New York: For a number of years I have been impressed, in reading the literature on brain tumors, by the frequent mention of the occurrence of mental symptoms, and yet as I have read the descriptions of the mental symptoms, I have always been left with a feeling that there had been really no adequate study of the psyche. For a long time at the Mount Sinai Hospital I have paid rather close attention to the character of the mental symptoms occurring in cases of tumor of the brain. Consequently, some years ago I asked my associate Dr. Keschner and my former resident physician Dr. Bender to make a survey of the mental changes in all our patients with tumor of the brain, starting with those who had tumor of the frontal lobe. This survey included not merely the clinical manifestations but a comparison of the clinical manifestations with the extent of the neoplasm, as shown either at operation or at necropsy. We intended to find out whether the involvement was only of the frontal lobe or whether there were pathologic changes in adjacent parts of the brain. The study today completes our investigation of this subject. I must admit that I was frankly surprised at finding that a large number of the patients with subtentorial tumor exhibited disturbances of the psyche. I had always been under the impression, as have most neurologists, that patients with tumor of this localization rarely

exhibit mental symptoms. When it was shown to me that there was such a large percentage exhibiting disturbances of a mental character, I felt that these manifestations were probably due to the increase in intracranial pressure which is almost invariably present. However, it is to be noted that this cannot be the only explanation and that intracranial pressure is only one of the factors producing the mental changes.

Dr. Schilder is correct in stating that it would be extremely important if one could make an exhaustive psychologic study of these patients. In this way one might obtain a great deal of insight into the changes that take place in the total personality of a person in whom there is a tumor of the brain. But there is a difficulty in making such a study: These patients come to a service, a neurologic service, for operation because life is in danger, and no neurologist wishes to delay operating on such a patient any longer than is necessary for him to make the diagnosis and localize the tumor. A study such as Dr. Schilder proposes would require, in my opinion, a longer period of observation before operation than would be warranted. There are certain patients on whom such a study might be made and operation delayed, but when it is remembered that a patient with a tumor of the brain can die suddenly, it makes it important to avoid unnecessary delay. I think that is one of the big difficulties which would be encountered if one tried to follow out the excellent and necessary program which Dr. Schilder proposes.

Dr. S. Bernard Wortis, New York: I think this paper is one of the most valuable contributions heard at this meeting. One certainly must revise some of one's old ideas of localized function of the brain which came from the days of phrenology. One is presented with the fact that tumor in the posterior fossa can produce mental aberrations in behavior, often similar to those associated with a supratentorial tumor.

It appears to me that perhaps one should look on tumor of the brain of a definite localization not as producing a definite symptom but as leaving a definite defect in the personality make-up.

Studies of the psychopathologic processes in adults having tumor of the brain would be very valuable in helping to determine the origin and perhaps the location of some of the psychic mechanisms one sees uncovered in these patients.

Dr. Richard N. Brickner, New York: I also should like to express appreciation for the painstaking work which the paper of these investigators represents. A remark on the question of the symptoms that are caused by increased intracranial pressure might be relevant. This factor seems to be a puzzle whenever the question of mental symptoms in patients with tumor of the brain arises. There have been observers, particularly in Europe, to whom the destruction of tissue seemed to be quite unimportant in the production of mental symptoms. They have held that all the symptoms may be due to elevated intracranial pressure or to toxemia of the brain caused by the tumor or that the tumor is acting as a foreign body to which the rest of the brain is reacting. These theories have implied complete neglect of the fact that large amounts of brain tissue are destroyed.

Recently, however, the rôle of increased intracranial pressure has been more carefully weighed and to a considerable extent clarified by Baruk and other French authors and by Puusepp of Rumania. It appears from the work of these investigators that the only symptoms that can be depended on as being due to increased intracranial pressure are confusion, stupor and general lowering of intellectual and emotional vis a tergo. This work is not very well known in America, and it might be worth while if it were stressed.

Dr. Moses Keschner: We agree with Dr. Schilder that it would be desirable to investigate the dynamics of the mental symptoms in patients with tumor of the brain. We hope to pursue this problem further in the near future.

Regarding Dr. Brickner's remarks, we discussed in detail the pathogenesis of the mental symptoms in patients with tumor of the brain in our first contribution on this subject. In our paper on the mental symptoms in patients with tumor of the frontal lobe we pointed out the respective rôles played by intracranial hypertension, primary destruction of brain tissue by the tumor itself and the secondary changes from interference with the circulation giving rise to necrosis in the neural structures immediately adjacent to and even remote from the tumor.

FORMS OF FAMILIAL ATAXIA RESEMBLING MULTIPLE SCLEROSIS

A CLINICAL STUDY

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AND
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Amid prolonged discussion of the etiology, pathologic characteristics and treatment of multiple sclerosis, its clinical study has been neglected. Diagnosis of the disease has become a trite exercise, reserved for beginners. Yet to one with experience the extreme variability of the symptomatology makes the diagnosis a distinct problem. The famous triad of Charcot—nystagmus, intention tremor and scanning speech—means only disease of cerebellar connections and may appear in several conditions. In cases in which there are onset at an early age, definite remissions and undoubtedly disseminated lesions, leading eventually to incapacitation, there is not often much debate, but the incomplete syndromes, the apparently arrested forms and, particularly, the nonremittent, progressively paraplegic types lead to much confusion.

Wide divergences in symptomatology between "typical" cases make it probable that multiple sclerosis as it is diagnosed at present may in reality represent several morbid entities. An attempt to delimit some of these groups and to identify their clinical characteristics can serve only to clarify concepts of the disease. Although pathologic study must form the ultimate criterion, careful clinical analysis is indispensable. In the present report, a purely clinical approach has served to identify two forms of familial ataxia frequently, but unjustifiably, diagnosed as multiple sclerosis. In the majority of cases reported in this paper qualified neurologists had made this diagnostic error.

FRIEDREICH'S ATAXIA

The D. Family.—CASE 1.—P. D., a woman aged 46, unmarried, was admitted to the Cook County Hospital in November 1935. She had repeatedly been a patient in this hospital, and her disease had been diagnosed by outstanding neurologists as multiple sclerosis, often with the prefix "typical" or "classic." It was not until this occasion, however, that it was learned that her sister (Mrs.

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From the Departments of Neurology, the St. Luke's Hospital and the Research and Educational Hospital, University of Illinois.

R., case 2) had the same affliction. The family history was otherwise without significance.

At the age of 11 years the patient began to suffer from ataxia in all four extremities, which increased progressively. She had been practically unable to walk for six years and had had occasional incontinence of urine. Speech had gradually become disturbed.

Neurologic examination (Feb. 1, 1936) revealed marked nystagmus, slurred and scanning speech and a definite intention tremor. The handwriting was markedly ataxic (fig. 1). There was spastic weakness of all four extremities; all the tendon reflexes were exaggerated except the ankle jerk, which was absent on both sides, and there was patellar clonus bilaterally. The Hoffmann and Babinski reflexes were strongly positive bilaterally, and the abdominal reflexes were absent. The gait was markedly ataxic and moderately spastic; the Romberg sign was strongly positive, and there was extreme adiadokokinesis. Common sensation was normal everywhere; vibratory sense was absent below the iliac crests, and the sense of position was reduced in the toes. There was no scoliosis; the plantar arches were moderately high. All laboratory findings, including those of the spinal fluid, were normal.

Case 2.—Mrs. R. (a sister of P. D.), aged 58, a resident of Los Angeles, in whose case the history of the illness and the results of neurologic examination were furnished by Dr. Samuel D. Ingham, had never been robust; she was essen-

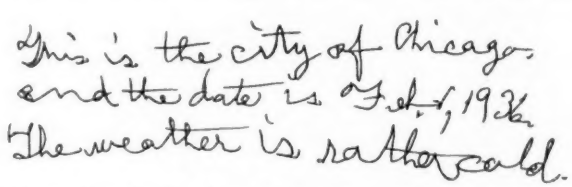


Fig. 1 (case 1).—Handwriting of a patient with Friedreich's ataxia.

tially normal until the age of 28, when she began to have progressively increasing difficulty in walking, disturbances in speech and tremors. At the time of examination by Dr. Ingham she could walk only with assistance.

Neurologic examination revealed slight pallor of the left optic disk and marked horizontal and vertical nystagmus, with poor convergence. There were scanning speech and definite intention tremor, with incoordination and adiadokokinesis in both arms. The extremities were all spastic and ataxic, but there was no paralysis. The tendon reflexes were absent in the arms; the patellar reflexes were brisk, and the ankle jerks were absent. The Babinski sign was strongly positive on both sides; the abdominal reflexes were not reported. Sensation was said to be normal, but there was no record of a study of vibration and joint sense.

There is little doubt that these two sisters suffered not from multiple sclerosis but from Friedreich's ataxia. This opinion rests on the early age at the time of onset (11 years) in one sister, the prolonged duration of the illness, the slowly progressive rather than remittent course, the absence of the ankle jerk, the presence of pes cavus in one sister and, chiefly, the familial incidence. That final diagnosis must await neurohistologic study is admitted. A case recently reported by Brouwer [1]

1. Brouwer, B.: Ueber eine besondere, der Friedreichschen Tabes nahestehende Form familiärer Sclerosis multiplex, Ztschr. f. d. ges. Neurol. u. Psychiat. **148**: 321-334, 1933.

demonstrated that what appears to be Friedreich's ataxia may be proved eventually to be multiple sclerosis, but it is sufficient here to show how remarkably similar the two diseases may be and how the criteria mentioned may be utilized in distinguishing them. We wish to emphasize that in cases in which the diagnosis is questionable the early age at onset, progressive rather than remittent course, reduction or absence of the achilles reflex and familial incidence, as well as skeletal changes, speak for Friedreich's ataxia.

FAMILIAL CEREBELLAR ATAXIA

The V. Family.—CASE 3.—F. F. V. Sr., a white man aged 39, an electrical engineer, was referred to us by Dr. James F. Cox on May 21, 1931. The family history was reported as without significance, except that a sister, aged 44, was "nervous." The patient was married and had two healthy sons, aged 16 and 14 years. There had also been two prematurely born children who had died shortly after birth.

For an indefinite number of years the patient had noticed a tremor of the hands when writing or drinking from a glass. For two years he had had slowly progressive unsteadiness in walking, noticed by others as well as by him. He began at about the same time occasionally to see double when reading; he had prisms fitted. One year before our examination a physician for a life insurance company had pronounced the legs "spastic" and the reflexes "too active." There were gradually increasing stiffness and awkwardness of the legs, so that it became difficult for him to walk downstairs. There had been no disturbances of the sphincters, no sensory abnormalities and no difficulty in speaking.

Neurologic examination revealed slight exophoria, with bilateral horizontal and vertical nystagmus. The functions of the cranial nerves, including speech, were otherwise normal, though there was slight obstructive deafness on the left. There was definite intention tremor of both hands in all movements of precision; the handwriting was ataxic (fig. 2). No motor weakness was found, but both legs were slightly spastic, and all tendon reflexes were brisk, with three strokes of ankle clonus on each side. The abdominal reflexes were present but sluggish bilaterally. The Hoffmann sign was absent; reaction to the Babinski test was equivocal on both sides. The gait was definitely ataxic and appeared somewhat spastic. Adiadokokinesis of moderate degree was present in both upper extremities. The Romberg test revealed slight swaying. All forms of sensation, including vibration and position sense, were normal. Examination of the blood and spinal fluid gave normal results.

The probable diagnosis was an atypical form of multiple sclerosis, which was progressive rather than remittent.

Course: We saw no more of this patient until Nov. 12, 1935. In the interim he had been examined at two university hospitals, where a diagnosis of multiple sclerosis was made. He had, however, made investigations regarding various members of his family and had discovered that several were similarly affected, to varying degrees (fig. 3).

Neurologic examination at this time revealed that in the interval there had developed a definitely explosive, ataxic and slightly slurred form of speech. The nystagmus, intention tremor, ataxic gait and handwriting had persisted unchanged, but the Babinski sign was absent. Vibration and joint sense remained normal; the abdominal reflexes were still present.

A description of other members of this interesting family follows:

CASE 4.—H. A. S. (maternal grandmother of F. F. V. Sr.) had had "nervous trouble" and eventually became helpless. No details were obtained except that the trouble was of a nervous character and that she died in an institution for patients with nervous disease, at the age of 65.

CASE 5.—S. E. V. (mother of F. F. V. Sr.) at the age of 41 began to stagger when walking. Speech also became jerky and slurred, worse than that of her

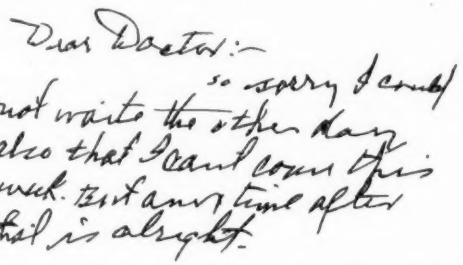


Fig. 2 (case 3).—Handwriting of F. F. V. Sr., who suffered from a form of familial cerebellar ataxia—probably olivopontocerebellar atrophy.

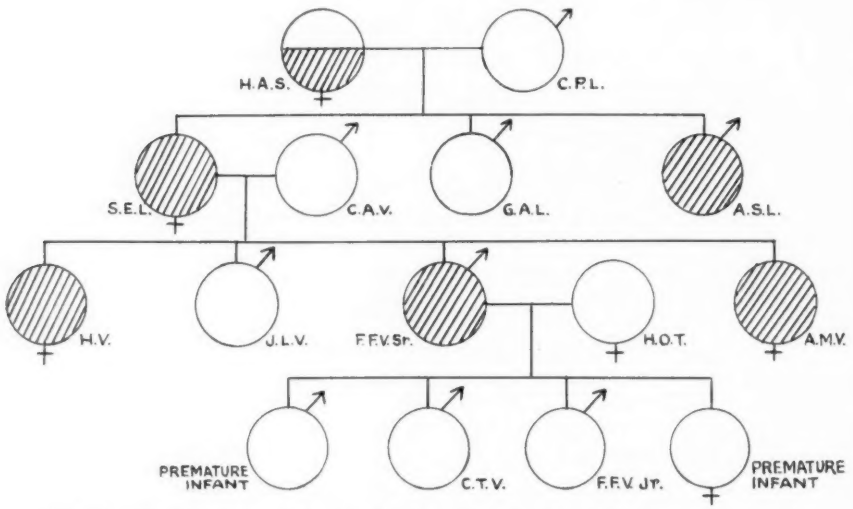


Fig. 3.—Family chart of the V. family. The shaded circles represent members affected with familial cerebellar ataxia. The condition of H. A. S. is doubtful.

son, and her handwriting became laborious and jerky (fig. 4*A*). She always covered one eye when viewing objects at a distance, and her eyes were said by an oculist to "jerk." She never became helpless, but her friends said that she had "slow paralysis." Eventually one arm and the homolateral leg became worse, and she fell frequently. She died at 71, of pneumonia.

CASE 6.—A. S. L. (maternal uncle of F. F. V. Sr.), aged 77 at the time of writing, a resident of Honolulu, H. I., began at an indefinite date, "many years ago," to have explosive, thick speech and somewhat ataxic handwriting. His gait

was also ataxic. Dr. F. J. Halford, of Honolulu, examined him and made the following observations: The gait was a "jumpy, up and down movement," requiring the use of a cane. An old fracture of the right hip, sustained seven years before, made walking still more difficult. Speech was a series of explosive words or sentences, coupled with thickened speech. The handwriting was slow and somewhat ataxic (fig. 4 *B*). The pupillary reflexes were normal, but no statement was made as to nystagmus. There was no paralysis, and all tendon reflexes were exaggerated; the abdominal and cremasteric reflexes were present; ankle clonus was absent, and the Babinski response was absent. The Romberg test revealed

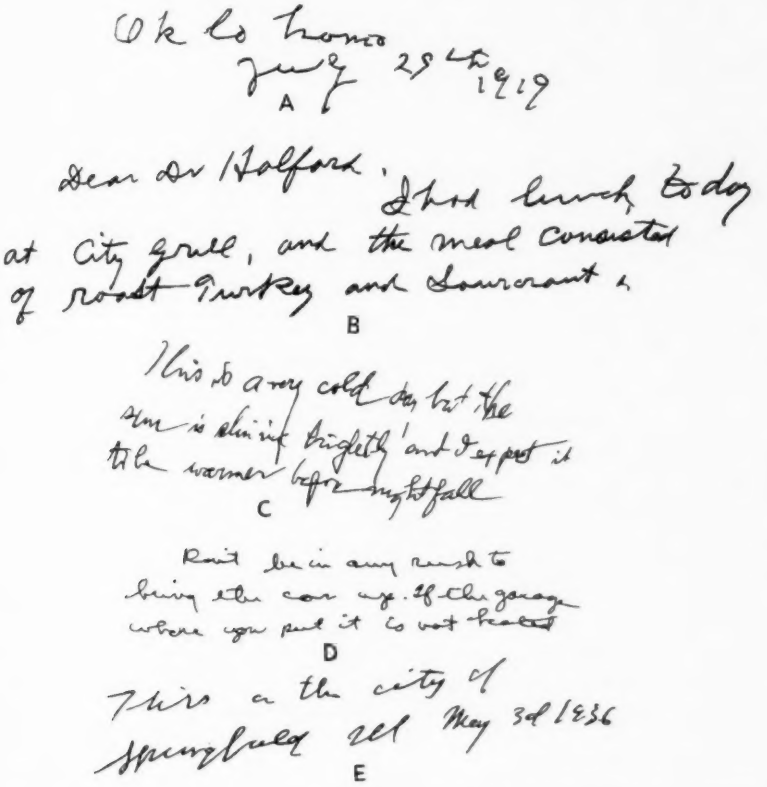


Fig. 4.—Handwriting of various members of the V. family, who were probably afflicted with olivopontocerebellar atrophy. The text contains a detailed report.

no abnormality. All forms of sensation, including temperature and vibration sense, were normal.

CASE 7.—J. L. V. (a brother of F. F. V. Sr.), a traveling salesman aged 50, had always had rapid, somewhat explosive speech, with occasional slurring. His handwriting, likewise, was always "terrible." He had a daughter, aged 21, who was normal at the time of writing.

Examination on May 3, 1936, revealed quick, explosive, occasionally slurred speech and very careless and rapid, though not definitely ataxic, handwriting (fig. 4 *E*). There were no other neurologic abnormalities. The gait was quick

and "pert" but not ataxic. The Romberg sign was absent; nystagmus, intention tremor and other "cerebellar" signs were not found.

CASE 8.—H. V. (a sister of F. F. V. Sr.), an unmarried school teacher, aged 48, living in the state of New York, had had occasional pains in the arms and legs since the age of 32 years. At 34 she had a severe attack of septic sore throat and was depressed because of the death of her mother (S. E. V., case 5). At 43 she had a severe hemorrhage after the removal of a few nasal polyps; secondary anemia and decrease in weight (from 130 to 108 pounds [59 to 49 Kg.]) followed.

About that time her handwriting, which had formerly been rapid and good, became jerky and unsteady and grew rapidly worse. A year later (1933) speech also became jerky and unsteady and thereafter grew progressively worse, almost to the point of being indistinguishable. She was much more dysarthric when tired or in a hurry. A year later (1934) a friend told her that her gait was awkward; this likewise became gradually worse. A physician in New York made a diagnosis of multiple sclerosis.

Neurologic examination on Dec. 29, 1935, revealed definite horizontal nystagmus and slurred and ataxic speech, but no marked intention tremor in the usual clinical tests, although there was unsteadiness of the right hand in holding a glass of water. The handwriting was characterized by typical cerebellar ataxia (fig. 4 *C*). The patient walked with a wide base and staggered, especially on turning suddenly. There was no paralysis. The tendon reflexes were all present and equal on the two sides of the body, but the knee and ankle jerks were sluggish. The abdominal reflexes were brisk on both sides; no pathologic reflexes or clonus was elicited. Sensation, including not only common sensation but position and vibration sense, was normal.

CASE 9.—A. M. V. (a sister of F. F. V. Sr.), single, a trained nurse aged 41, made no complaints but had noticed the necessity of closing one eye in order to avoid seeing double when looking to one side. She had been teased by medical friends because the knee jerks were said to be absent.

Neurologic examination revealed definite but rather poorly sustained vertical and horizontal nystagmus. There were poor ocular convergence and a tendency to exophoria, with crossed diplopia in gazing far to either side. There was a tendency to speak fast and indistinctly, with occasional slurring. No intention tremor was detected, but the handwriting was slightly ataxic (fig. 4 *D*). Gait was normal, but she hopped somewhat awkwardly on either foot. No adiadokokinesis was detected. There was no paralysis. All tendon reflexes were present but sluggish, the biceps, knee and ankle jerks being obtained only with reenforcement. The abdominal reflexes were likewise sluggish but were consistently present. No pathologic reflexes were elicited. All forms of sensation, including touch, pain, temperature, vibration and joint sense, were normal.

CASE 10.—F. F. V. Jr. (a son of F. F. V. Sr.), a high school student aged 16, made no complaints. Examination revealed only rather high plantar arches, slight intention tremor, with a suggestion of ataxia in the handwriting, and brisk tendon and abdominal reflexes, without clonus or pathologic reflexes.

CASE 11.—C. T. V. (a son of F. F. V. Sr.), a student aged 20, also made no complaints. Examination revealed no abnormalities except definitely brisk tendon reflexes and rather sluggish but equal abdominal reflexes on the two sides. The handwriting was normal.

In this family there can be little doubt as to the presence of a familial type of so-called cerebellar ataxia. The manifestations were remark-

ably constant, almost stereotyped, in F. F. V. Sr. (case 3), in his mother (case 5), though the data were incomplete for the latter, and in his sister (case 8). The maternal grandmother (case 4) had a progressive neurologic disease, but information was lacking as to her true condition. In a maternal uncle (case 6), who is aged 77 at the time of writing, the disease must have run its full course, though its manifestations were only partial; in a younger sister (case 9) the incomplete picture was indubitable and may be filled out more fully with the passage of time. A brother (case 7) showed speech and handwriting which suggested cerebellar ataxia, but he could hardly be said to suffer from the disease. The disease in its most complete form, as shown in cases 3 and 8, was characterized by ataxic gait, slurred, scanning and ataxic speech, intention tremor, with characteristically ataxic handwriting, and definite nystagmus. With these "cerebellar" signs there was no real evidence of disease of the spinal cord; i. e., there were preserved or brisk tendon and abdominal reflexes, absence of pathologic reflexes and lack of sensory disturbances. Atrophy of the optic nerve formed no part of the syndrome in this family, and the progress of the disease was steady rather than remittent. In spite of this syndrome, a diagnosis of multiple sclerosis had been made in several of the persons involved.

The disease in the next two families follows this general pattern:

The M. Family.—CASE 12.—H. Y. (née H. M.), a married woman aged 23, was referred to the neurologic service of the Research and Educational Hospital by Dr. John R. Dwelling on Dec. 13, 1935, with the complaint of unsteadiness of gait and handwriting for two years and slight difficulty in speech for nine months. Her father had died at 62 of malignant disease; her mother, aged 62, was living and well. A brother (F. M., case 13), aged 30, had had staggering gait for fifteen years; a sister, aged 35, had had visual difficulty for ten years but could read with glasses. Another brother, aged 25, and two other sisters, aged 32 and 28, respectively, were normal.

Though the patient had been married for four years, she had never been pregnant and had not menstruated for seventeen months. Her general health had always been good. She had skipped a rope well as a child and had played volley ball until she was 18 years of age. A mild attack of influenza in 1932, at the age of 20, had left no sequelae.

Two years before her admission to the hospital, at the age of 21, the patient had begun to suffer from gradually increasing unsteadiness of gait. She lost balance easily and almost fell when turning quickly. She seemed to stagger worse in the dark. At about the same time she began to have unsteadiness of the hands, which progressively grew worse and finally made writing difficult; it reduced speed in typing from ninety to thirty words a minute. Slight difficulty in speech appeared nine months before her admission.

General physical examination showed nothing abnormal except that the uterus was the size of a thimble, which explained the amenorrhea.

Neurologic examination revealed slight dysarthria, not definitely of abnormal degree. There was no nystagmus. Moderate intention tremor was present in all extremities, and the handwriting was definitely ataxic (fig. 5*B*). Adiadoko-

kinesis was present in both hands but was more marked on the left. The gait was sufficiently ataxic to prevent walking heel to toe or hopping on either foot. There was no paralysis or sensory disturbance; all the tendon reflexes were slightly increased and equal on the two sides. The abdominal reflexes were normal; no pathologic reflexes were elicited. There was slight swaying in the Romberg test. All laboratory tests gave normal findings, including those of the spinal fluid. Perimetric examination of the visual fields revealed nothing abnormal.

CASE 13.—F. M. (a brother of H. Y.), aged 30, single, a farmer, came for examination at our request after we had seen H. Y. His past medical history was without significance. When 12 years of age he had begun suddenly to stagger in walking and fell once on the way to school. Since, the gait had grown progressively more unsteady but had seemed almost unchanged during the past five years. When 15 he could no longer run well or play ball; his hands began to be unsteady in all fine movements; his handwriting was very poor, and diplopia occurred occasionally.

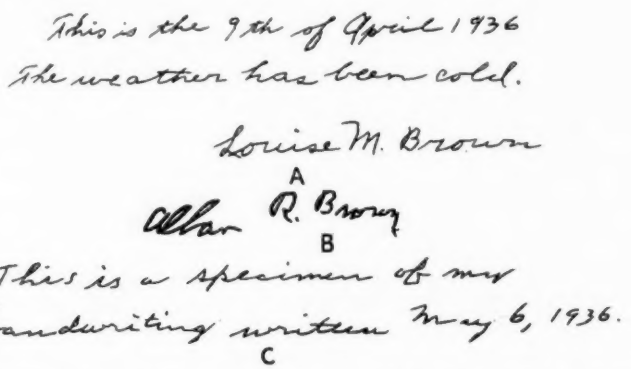


Fig. 5.—Handwriting of various members of the B. family, who were probably afflicted with olivopontocerebellar atrophy. The text gives a detailed report.

Neurologic examination on Jan. 7, 1936, revealed vertical and horizontal nystagmus, but no ocular palsy. Speech was markedly slurred and scanning. Intention tremor was seen in the finger to nose test on both sides, and there was definite adiadokokinesis in both hands. The gait was markedly ataxic and slightly spastic, and the patient walked with a wide base. The handwriting was ataxic (fig. 5*A*). He could not stand with his feet together, with the eyes either open or shut. There was no paralysis, but a suggestion of hypertonus was present in all extremities. All forms of sensation were normal. All tendon reflexes were brisk and equal on the two sides of the body; the abdominal reflexes were present. The Hoffmann, Babinski, Chaddock, Rossolimo and Mendel-Bechterew tests elicited normal responses, but the Oppenheim reaction was equivocal. All laboratory tests, including those of the spinal fluid, gave normal results.

The close resemblance of the symptoms in these two siblings to those in the V. family is obvious. Again there were "cerebellar" signs in the form of ataxic gait, speech and handwriting, intention tremor, adiadokokinesis and nystagmus. The syndrome was more complete in the brother but was unmistakable in the sister. Atrophy of the optic nerve again

was lacking, and no evidence of disease of the pyramidal tract or sensory disturbance was present. Once more, the progress of the disease was steady rather than remittent.

The B. Family.—CASE 14.—L. M. B., a single woman aged 37, began as early as 1922, when 23, to have difficulty in dancing and thereafter became gradually more unsteady in walking. By 1930 she had become unable to walk without assistance. In 1932 the hands became unsteady in all fine movements, and the handwriting was jerky. In 1933 speech became stumbling and jerky, and she had especial difficulty in repeating syllables such as "kitty, kitty, kitty." The dysarthria grew progressively worse. In 1932 she often choked because food or fluids passed into the larynx. There was no regurgitation into the nose. This symptom disappeared after a few months. Recently, a slight rhythmic tremor appeared in the right hand while at rest.

In July 1935 a neurosurgeon made a diagnosis of multiple sclerosis but then changed his mind. He performed "cervical sympathectomy" on the right side, after which the patient thought she was improved somewhat.

Two brothers (E. C. B. and A. R. B.), both older than the patient, suffered from similar symptoms. One sister was living and well, while another sister died at 45, without having presented any neurologic symptoms.

Neurologic examination (April 9, 1936) revealed a definitely slurred and stumbling speech, which was of uneven expulsive force, explosive in some syllables and of scanning type. There was intention tremor in the arms in such acts as lighting a cigaret, and it was more marked in the heel to knee test. Adiadokokinesis was present to a moderate degree in both hands. The handwriting (fig. 6 *A*) was somewhat ataxic and was laboriously done. The gait was markedly ataxic; the patient could barely walk without a cane, and turning was especially difficult. She swayed with her heels together, whether the eyes were open or closed. There was no motor weakness, but muscular tone was slightly increased in all extremities. There was a slight rhythmic tremor in the right hand when at rest, closely resembling the parkinsonian type. All tendon reflexes were brisk; the abdominal reflexes were normal; the plantar response was flexor. All forms of sensation, including position and vibration sense, were preserved. (There was no ocular evidence of cervical sympathectomy on the right.)

CASE 15.—A. R. B. (a brother of L. M. B.), aged 53 at the time of writing, an attorney in New York City, was seen in 1920, 1921 and 1926 by Dr. Israel Strauss, who furnished the following data:

The past history was essentially without significance. The patient was married and in 1920 had two living children. In 1919 the Wassermann reaction of the blood was negative. He had begun in 1916 (age 33) to have difficulty in walking.

Examination by Dr. Strauss in 1920 revealed ataxic gait, with a broad base, and some ataxia in the left hand. There was no nystagmus or disturbance in speech. All reflexes were active. An inconstant tendency to a Babinski sign on the right was suggested. There were no disturbances in position or vibration sense. Roentgenograms of the head and spine revealed nothing abnormal.

In 1921 the patient seemed somewhat improved, and the Babinski sign was recorded as absent.

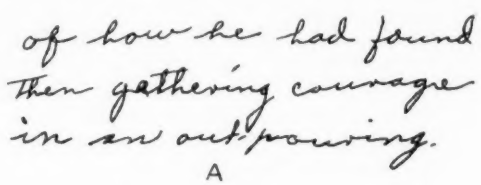
When next seen in 1926 (aged 43) he was much worse. There was still no nystagmus, but speech was ataxic and scanning. The optic nerves were normal. The arms were slightly ataxic, and the gait was markedly so. Involuntary move-

ments of the head and trunk were also ataxic. The Babinski sign was again suggested, but all other reflexes, including the abdominal, were normal, and all forms of sensation were intact.

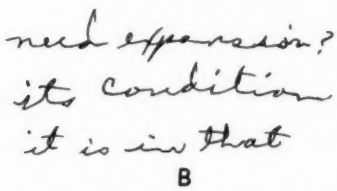
In Dr. Strauss' opinion the patient had familial cerebellar ataxia. We have no further detailed information regarding this patient, except that he is still active as an attorney at 53. His handwriting is shown in figure 6 *B*.

CASE 16.—E. C. B. (a brother of L. M. B.) lived in Tulsa, Okla., and the following data were furnished by Dr. Donald McCarthy, of Minneapolis, who has known the family for years and examined the patient ten years ago.

The patient, aged 49, was married and had six normal children, the youngest being 15 years old. The past history was without significance except for frequent "cramps" of the feet at the age of 20 years. In 1925, when 38, he began to be unsteady in walking and had to think constantly of his feet. He could not move his feet fast enough to run upstairs. There was no more trouble in walking in the dark than in the light. The condition progressed gradually.



A



B

Fig. 6.—Handwriting of F. M. and H. Y., brother and sister in the M. family, who probably suffered from olivopontocerebellar atrophy.

Examination by Dr. McCarthy on Sept. 22, 1926, when the patient was 39, revealed an ataxic gait, with a wide base. There was no disturbance of the ocular movements or incoordination in the upper extremities, though there was some incoordination in the lower. In the Romberg test he tended to fall backward and to the left. No mention was made of any form of disturbance in speech. There was apparently no motor weakness; the tendon reflexes were all present and somewhat increased, with bilateral patellar clonus but no ankle clonus. The abdominal reflexes were brisk and equal on the two sides, and the Babinski, Chaddock and Oppenheim tests all gave plantar flexion. All forms of cutaneous sensibility were normal, but there was reduction in vibration sense at the ankles.

All laboratory tests, including those of the urine and blood and the Wassermann tests of the blood and spinal fluid, gave normal results.

Dr. McCarthy saw the patient again in the autumn of 1935 but had no opportunity to examine him. There had been no great progression of the condition. His handwriting is shown in figure 6 *C*.

These three siblings presented the same almost stereotyped syndrome, which need not be further described. The sister, L. M. B., duplicated the pattern shown by the first patient (case 3) in our series except

for nystagmus, which was absent in the whole B. family. In all other particulars one sees again the combination of "cerebellar" signs and sparing of the spinal cord. The progress of the disease again was steady rather than remittent. In spite of this pattern, a diagnosis of multiple sclerosis in the sister was made on one occasion.

GENERAL COMMENT

The chief point of interest in the cases reported lies in the fact that in many instances the disease was mistaken for multiple sclerosis. As regards Friedreich's ataxia, this mistake is almost unavoidable when no familial incidence is known and scoliosis or pes cavus is not present. The combination of nystagmus, scanning or ataxic speech, intention tremor and adiadokokinesis, with signs of involvement of the pyramidal tract and loss of proprioceptive and vibratory sensibility, cannot fail to suggest multiple sclerosis. Friedreich's ataxia should be suspected when the onset occurs at an early age and the course of the disease is steadily progressive rather than remittent. In our opinion the disease today is wrongly diagnosed as multiple sclerosis in many cases through disregard of these criteria.

In the cases of familial cerebellar ataxia which we have described this condition also was frequently wrongly diagnosed. We believe that our diagnosis of cerebellar ataxia in these cases cannot be seriously doubted, provided that they are considered in the aggregate. If the cases were considered individually and without knowledge of the familial incidence, mistakes might conceivably occur. Analysis of the symptomatology in these cases leads us to emphasize the following points of differentiation:

1. In all cases the age of onset was in early adult life, as in patients with multiple sclerosis, but the course was uniformly progressive and not remittent. In many of the patients the disease reached a stationary level, beyond which it seemed not to progress. There is a question in our minds whether one should not look with suspicion on the diagnosis of multiple sclerosis when the course of the disease is uniformly progressive.

2. Evidence of disease of the spinal cord was practically absent in all the cases in our series. Most of the patients showed brisk tendon reflexes, and a few presented patellar or ankle clonus, but the abdominal reflexes were not absent and pathologic reflexes were never elicited. Furthermore, no diminution of vibration sense was found in any instance. It seems to us that absence of the Babinski sign and of other pathologic reflexes and the presence of unimpaired proprioceptive and vibratory sensibility should exclude the diagnosis of multiple sclerosis, especially in a stage sufficiently advanced to produce scanning speech, intention tremor and nystagmus. There is perhaps an early stage in certain cases of multiple sclerosis in which evidence of involvement of

the spinal cord is absent, but at this stage the disease probably cannot be diagnosed.

3. The familial incidence in these cases speaks against multiple sclerosis. We have seen one or two instances of familial multiple sclerosis, but such cases are probably not more frequent than can be explained on the basis of coincidence. The recent studies of von Hoesslin [2] and Curtius [3] were far too uncritical and unconvincing to have much weight. It is indeed probable that these investigators fell into an error similar to that with which we are at present concerned, viz., the mistaking of a form of familial ataxia for multiple sclerosis. It should be emphasized that no study of familial multiple sclerosis can have real value unless a strict concept of multiple sclerosis can be observed and the diagnosis firmly established in each case. The same objection holds good in any statistical study of multiple sclerosis for the purpose of drawing conclusions regarding the results of treatment. Such a study, often utilizing the work of numerous observers, is in danger of being vitiated by varying and confused diagnostic criteria. The frequency with which the wrong diagnosis was made in some of the cases reported in this paper illustrates this danger.

In the cases of familial cerebellar ataxia we have reported it is difficult to label the condition with a diagnostic name. A comparison with similar reports in the literature leads us to believe that they are instances of olivopontocerebellar atrophy. Originally thought to be nonfamilial,[4] this disease is now known to occur in families.[5] It was first clearly described by Dejerine and Thomas.[4a] Though a fair number of reports have been published, especially in the French literature,[6] the clinical features are less well established than the pathologic. The remarkable Drew family, described by Ferguson and Critchley,[7] was probably afflicted with olivopontocerebellar atrophy, though it is likely that other neurologic conditions confused the picture. It is interesting that Dejerine

2. von Hoesslin, Rudolf: Ueber multiple Sklerose: Exogene Aetiologie, Pathogenese, und Verlauf, Munich, J. F. Lehmanns Verlag, 1934.

3. Curtius, Friedrich: Multiple Sklerose und Erbanlage, Leipzig, Georg Thieme, 1933.

4. (*a*) Dejerine, L., and Thomas, André: L'atrophie olivo-ponto-cérébelleuse, Nouv. iconog. de la Salpêtrière **13**:330-370, 1900. (*b*) Holmes, Gordon: An Attempt to Classify Cerebellar Disease, with a Note on Marie's Hereditary Cerebellar Ataxia, Brain **30**:545-567, 1907.

5. (*a*) Keiller, W.: Four Cases of Olivo-Ponto-Cerebellar Atrophy Giving a History of Heredity, with Three Autopsies, South. M. J. **19**:518-522 (July) 1926. (*b*) Hassin, George B., and Harris, Titus H.: Olivopontocerebellar Atrophy, Arch. Neurol. & Psychiat. **35**:43-63 (Jan.) 1936.

6. A rather extensive bibliography may be found in the article by Hassin and Harris.[5b]

7. Ferguson, Fergus R., and Critchley, Macdonald: A Clinical Study of an Heredo-Familial Disease Resembling Disseminated Sclerosis, Brain **52**:203-225, 1929.

and Thomas devoted considerable space to the delicate differentiation between olivopontocerebellar atrophy and multiple sclerosis, while Thomas, in a later report,[8] described a case in which both conditions were observed at necropsy.

The original article by Dejerine and Thomas described cases remarkably similar to our own, in which there were ataxic gait and handwriting, nystagmus, intention tremor, scanning speech, increased tendon reflexes and absence of pathologic reflexes or sensory changes. Their patients also presented rhythmic tremors when at rest and spasticity of the extrapyramidal type. Other reports,[9] particularly those of Guillain and his associates, emphasized the presence of rigidity, although still others have not mentioned it. In the only case which we have observed in which the diagnosis was pathologically verified the patient presented a clinical picture resembling that of encephalitic parkinsonism, accompanied by "cerebellar" signs. In this connection it is interesting that one of our patients (case 14) had a definite though slight rhythmic tremor in the right hand when at rest.

We suggest, therefore, that in the cases of familial cerebellar ataxia which we have reported the disease probably belongs in the classification of olivopontocerebellar atrophy. This suggestion is, however, unverified at best and must remain so as long as no pathologic studies are available.

CONCLUSIONS

The present clinical conception of multiple sclerosis is probably sufficiently confused to include several morbid entities.

Two cases of Friedreich's ataxia are reported in which the disease closely resembled multiple sclerosis and had been frequently diagnosed as such by neurologists of good standing.

Three families are reported containing from two to five members afflicted with a form of cerebellar ataxia which was probably olivopontocerebellar atrophy.

The clinical resemblance of this disease to multiple sclerosis is close, but it can usually be differentiated by its progressive rather than remittent course, its tendency to spare the pyramidal tract and dorsal funiculus and its familial incidence.

8 South Michigan Avenue.

8. Thomas, André: Atrophie du cervelet et sclérose en plaques, Rev. neurol. **11**:121-131, 1903.

9. Guillain, Georges; Mathieu, Pièrre, and Bertrand, Ivan: Etude anatomo-clinique sur deux cas d'atrophie olivo-ponto-cérébelleuse avec rigidité, Ann. de méd. **20**:417-459 (Nov.) 1926. Guillain, Georges; Bertrand, Ivan, and Thurel, R.: Etude anatomo-clinique d'un cas d'atrophie olivo-ponto-cérébelleuse avec symptômes pseudo-bulbaires, Rev. neurol. **2**:138-154, 1933. Scherer, Hans Joachim: Extrapyramidale Störungen bei der olivopontocerebellaren Atrophie: Ein Beitrag zum Problem des lokalen vorzeitigen Alterns, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:406-419, 1933.

DISCUSSION

DR. WALTER D. SHELDEN, Rochester, Minn.: I have little to offer to resolve this dilemma. Opportunity was not given me to review the records for additional illustrations of this general problem. I am quite aware that the designation multiple sclerosis is applied to syndromes that vary greatly in rate, location and intensity. These variations provide abundant opportunity for mistakes.

It is not wise to make a diagnosis of multiple sclerosis without a reasonably protracted observation. A wide range of study is needed to recognize processes simulating multiple sclerosis. For example, studies of the blood, the spinal fluid, the visual fields and infectious processes may support or contradict the assumption that the condition in a given case is multiple sclerosis.

Dr. Hall and Dr. Mackay have emphasized sufficiently the importance of the clinical history of the patient and of his family stock as well. I agree with the authors that the attempt to express syndromes, etiologic factors and pathologic pictures of great variability by the term multiple sclerosis is vague and confusing. However, one can escape doing so only when an appropriate nomenclature is created by a broad and precise knowledge of this complex problem. This, it is hoped, may occur through research and experimentation.

PNEUMOGRAPHIC LOCALIZATION OF TUMORS OF THE BRAIN

I. TUMORS OF THE LOBES OF THE CEREBRUM

LORNE H. McCONNELL, M.D.
SASKATOON, CANADA
AND
ARTHUR E. CHILDE, M.D.
MONTREAL, CANADA

Believing that every one encounters difficulty in the interpretation of pneumographic roentgenograms outlining various portions of the ventricular system, we made a study of a group of cases of tumor of the brain. It is our opinion that a systematic and comparative analysis of any set of properly taken roentgenograms can reduce the error of interpretation almost to the vanishing point.

In this study of one hundred and twenty cases of tumor of the brain in which the diagnosis was verified, we have compared the roentgen films in each case with the normal ventricular outline and have made it possible visually to comprehend the situation on a printed form (fig. 1). This form as used as a routine is printed on the scale of one-half the original size. The upper row of diagrams represents the ventricles as we believe they appear when normal. Beneath this is a space in which the ventricular outlines are traced from the films by means of a pantograph. This instrument accurately reduces the size of the tracing to one half of the original size and retains the exact outline. The ventricles are inked in to correspond to the diagrams. When viewed from the side, the lateral ventricles are made solid black. When it is desired to show the opposite ventricle for comparison to illustrate the deformity more graphically, this ventricle is merely outlined. Below this appear three drawings of the skull in section, within which sketches of the tumor are made on the same scale for purposes of localization. Therefore, on a single sheet of paper one has a complete pneumo-ventriculographic study of the case.

From the Montreal Neurological Institute, McGill University.

The original report of this study was read before the meeting of the Neurological Section of the Montreal Medico-Chirurgical Society at Montreal, Canada, April 17, 1935.

MATERIAL

In this group of cases were included only instances of tumor of the brain in which the diagnosis was verified at operation or necropsy and which were classified pathologically. Air or oxygen had been injected directly into the ventricles in most instances, but in some cases the injection was made by the spinal route.

Selection of Tumors.—The drawings of the tumors and their particular shape and size were decided on after a careful study of the written operative reports (in the clinic with which we are associated operative reports are dictated immediately after the operation). When postmortem reports were also part of the record, these were used as additional evidence.

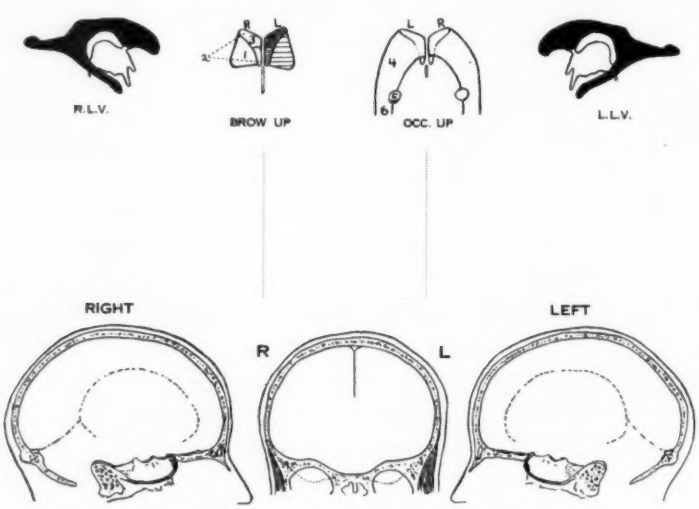


Fig. 1.—Pneumographic analysis form.

Only cases of tumor of the brain were used in which all or enough of the neoplasm had been removed to give the surgeon an accurate location of the tumor. In all cases the operations were performed by Dr. Wilder Penfield, Dr. William V. Coné or Dr. A. R. Elvidge.

ROENTGENOGRAPHIC PROCEDURE

We employ the following procedure: After the injection of air or oxygen the patient is taken immediately to the roentgenographic department, where, in the horizontal position, one anteroposterior and one lateral film with the brow up are taken. These are developed, and if there is sufficient gas in the ventricular system the following films are taken: posterior-anterior and lateral with the occiput up, right and left lateral stereoscopic and, finally, another anteroposterior. The final film is made for comparison with the first in case a certain amount of rotation may be present. If there is still doubt, other films are taken, particular care being used to place the head so that gas is allowed to ascend to the area suspected. Ample time and careful rotation of the head are always used.

At this clinic, for purposes of description and because they throw distinct air shadows, the lateral ventricles are divided into six portions. This method of

description was introduced by Torkildsen and Penfield[1] in 1933 (fig. 2). Briefly, examination of the figure shows:

Portion 1: The tip of the anterior horn as it passes laterally and downward.

Portion 2: The section of the lateral ventricle situated in front of the thalamus and posterior to portion 1. It is bounded mesially by the septum pellucidum and laterally by the caudate nucleus.

Portion 3: This shadow is darker in the anteroposterior view because it is the largest gas-filled space in the picture and portion 2 is superimposed on it. It is bounded laterally by the caudate nucleus and above by the corpus callosum.

Portion 4: This shadow is produced by the posterior part of the body, which curves backward, downward and laterally.

Portion 5: This shadow is cast by the posterior horn. If present, it is usually circular and dark and is placed slightly mesial to the edge of portion 4.

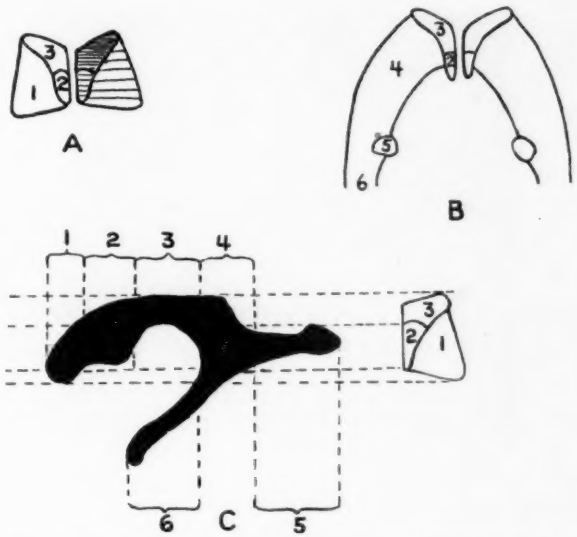


Fig. 2.—The lateral ventricles, modified from Torkildsen and Penfield.[1]

Portion 6: This shadow appears at a still lower level than portion 5 and represents the inferior horn.

A roentgenogram is submitted which shows clearly each of the portions named (fig. 3).

The general outline of the ventricles seen from the side is easily understood, and the portions are as shown in figure *2 C*.

We have found this method of description useful, and consequently it is employed throughout the analysis of the cases cited in this article.

DYNAMICS OF THE PRESSURE EXERTED BY TUMORS OF THE BRAIN

Before attacking the problem of the distinct lesions, it may be well to discuss briefly the dynamics of the pressure exerted by tumors and the manner in which this may be altered.

1. Torkildsen, Arne, and Penfield, Wilder: Ventriculographic Interpretation, Arch. Neurol. & Psychiat. **30**:1011-1021 (Nov.) 1933.

Because the brain is contained in a rigid structure, the skull, which cannot be expanded under ordinary conditions, any growing tumor within the cavity of the cranium must enlarge at the expense of the cranial contents. Many tumors of the brain are more or less spherical; they must, from the earliest moment of growth, exert their greatest pressure in the direction of greatest growth; this is, no doubt, redirected from time to time as the growth encounters structures of various density in its path.

The amount of force exerted by expanding lesions of neoplastic origin must vary with tumors of different density. Infiltrating tumors exert a different effect from those which are encapsulated.

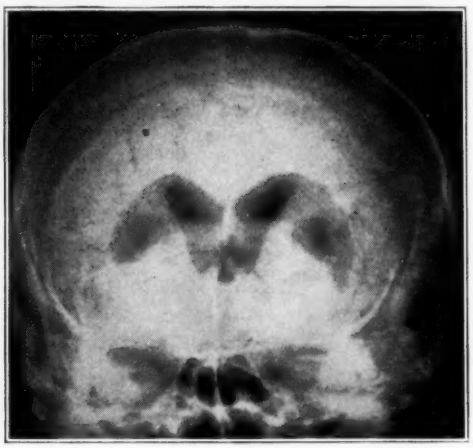


Fig. 3.—Roentgenogram showing portions 1, 2, 3, 4, 5 and 6 of the lateral ventricles, indicated in the diagrams reproduced in figure 2.

The pressure against the walls of the ventricles produces deformities. These distortions vary with the shape of the tumor and the distance of the tumor from the ventricle. The falx cerebri and tentorium act as comparatively rigid barriers to the direct application of pressure.

As has been pointed out by Cone [2] and also by Torkildsen and Pirie,[3] with special reference to tumors of the temporal lobe, the depression of the lateral ventricle in some cases may be explained by the redirection of the pressure. In other words, as the force is directed against the resistant falx it is redirected downward to the corpus callosum and depresses it. In addition, Cone has called attention to the possibility that flattening of portion 3 is due partly to the horizontal thrust of the brain under the falx.

2. Cone, W. V.: Personal communication to the authors.

3. Torkildsen, Arne, and Pirie, A. H.: Interpretation of Ventriculograms, Am. J. Roentgenol. **32**:145-153 (Aug.) 1934.

We believe that the caudate nucleus, the thalamus and the island of Reil concentrate and change the direction of pressure. Then, too, the irregular floor of the skull, with its fossae, alters greatly the growing direction of the tumor. Lastly, the edema of the brain, a frequent result of the growth, may cause greater dislocation of the ventricular system than the tumor itself.

ANATOMIC DISTRIBUTION

In the presentation of this study of cases of tumor of the brain we have defined the position of the growth on a purely anatomic basis. As is well known, a tumor of the brain frequently involves the adjoining lobes, and in such cases the tumor is described in the lobe which contains the greatest bulk of the growth.

Tumors of the Frontal Lobe.—The frontal lobe contains the part of the lateral ventricle which we describe as portions 1 and 2, as well as the anterior half of portion 3. The fissure of Sylvius and the fissure of Rolando meet at a point which, if projected horizontally inward, corresponds to a position just behind the interventricular foramina. It is evident, then, that in most cases a tumor of the frontal lobe will cause alterations in the form and position of the portions aforementioned, as well as changes in the position of the third ventricle.

A. Tumors of the Upper Posterior Part of the Frontal Lobe, Lying Against the Falx: Such a tumor, because of its position directly above the lateral ventricle, exerts its greatest pressure on its roof. In one half of the cases in this series no air was shown in the ipsilateral ventricle, though the third ventricle was visible. We believe, therefore, that the interventricular foramen on the side of the tumor is often collapsed. The third ventricle is concave toward the tumor, particularly in its upper portion. In the case of a very large tumor, the temporal horn may be flattened.

When the tumor penetrates the falx, the ipsilateral ventricle is distorted in portions 2 and 3. The opposite ventricle is pushed away, and the lumen of the interventricular foramen remains patent. It is our opinion that once the tumor erodes the falx a considerable percentage of the pressure is exerted in the lateral horizontal direction.

The falx cerebri is a fairly resistant curtain but is not immovable. When a tumor lies against the falx above the corpus callosum, the shift of the ventricular system must be the resultant of the resistance of the falx and that of the corpus callosum; as the resistance of the corpus callosum is considerably less than that of the falx, the ventricle will be displaced downward more than laterally. As already stated, however, when the falx is weakened by the invasion of the tumor more pressure is exerted immediately in a horizontal direction and less in a downward direction.

These findings are best seen in anteroposterior films. In lateral films one often sees an elongated curved "cut-out." This depression corresponds to portion 2 and part of portion 3; in the case of a large tumor portion 1 is also affected. The midpoint of the depression usually corresponds to the vertical diameter of the tumor and is therefore valuable in planning one's surgical approach.

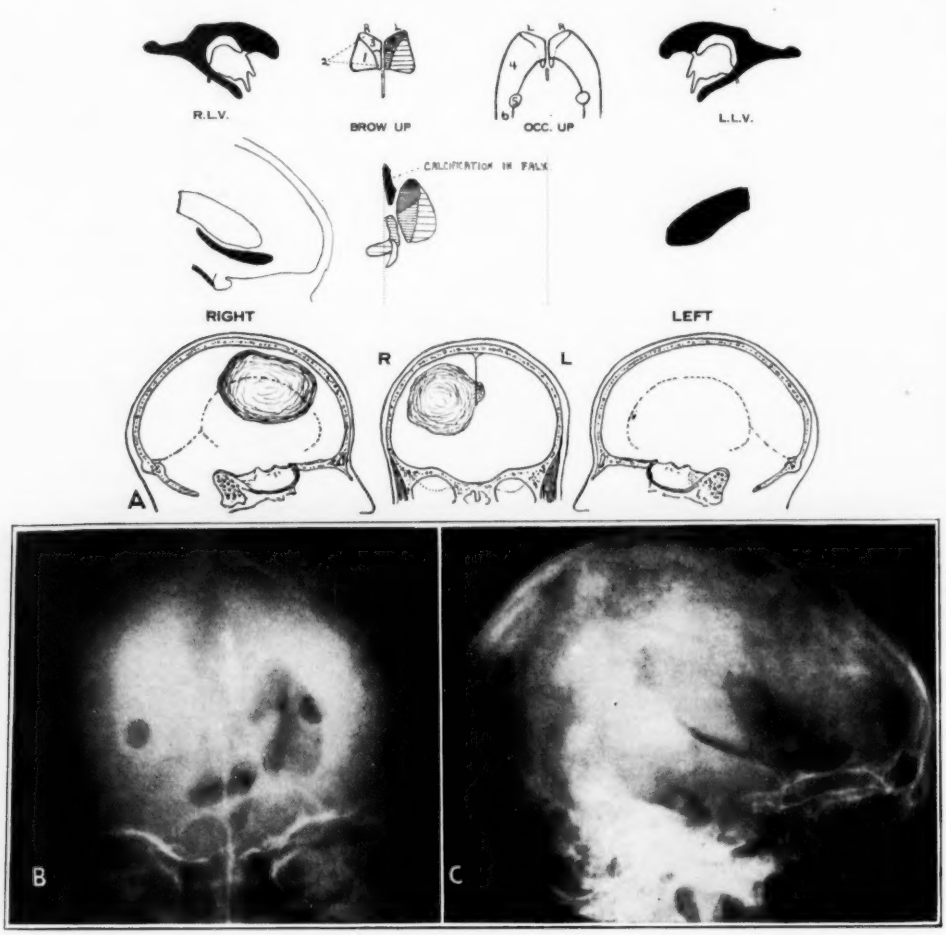


Fig. 4.—(*A*) Tumor of the upper posterior portion of the frontal lobe, lying against the falx, (*B*) anteroposterior roentgenogram used in making the tracing shown in *A*, and (*C*) lateral roentgenogram used in making the same tracing.

Case 1 (Mrs. J. H., aged 50; fig. 4 *A*).—Portions 1 and 2 and the anterior part of portion 3 of the right lateral ventricle are displaced downward and to the left and are also greatly compressed from above. Portions 1, 2 and 3 of the left lateral ventricle are dilated and displaced to the left. The third ventricle is similarly displaced and slightly concave toward the tumor. There is calcification in the anterior portion of the falx, to the left of the midline.

The entire tracing in this case was made from two films, both of which are reproduced (fig. 4 *B* and *C*). In many cases a number of roentgenograms were used to obtain the entire tracing, and a careful study of stereoscopic films was necessary, particularly in lateral views, to differentiate the shadows.

CASE 2 (Mrs. G. B., aged 35; fig. 5 *A*).—The filling is incomplete. Portion 1 of the right lateral ventricle is displaced to the right, much compressed from side

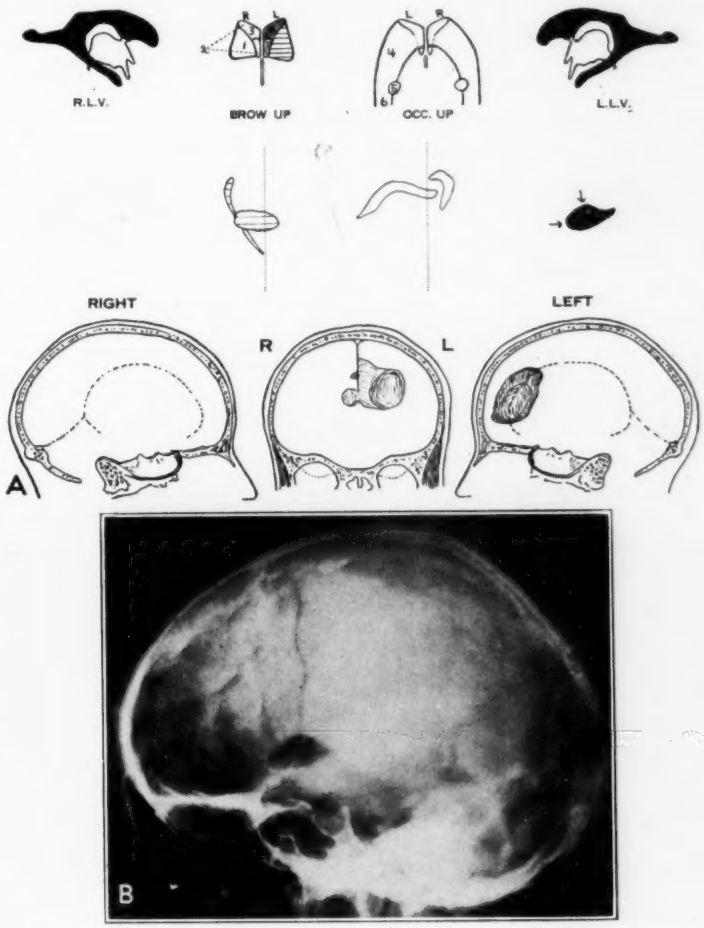


Fig. 5.—(*A*) Tumor of the upper posterior portion of the frontal lobe, lying against the falx and extending across the midline, and (*B*) roentgenogram used in making the tracing shown in *A*.

to side and concave toward the tumor. Portion 1 of the left lateral ventricle is flattened from above, depressed and displaced posteriorly and to the right. The third ventricle is of normal size but conspicuously displaced to the right.

The deformity of the left lateral ventricle is shown in the reproduction of the original film (fig. 5 *B*).

B. Upper Posterior Part of the Frontal Lobe—Away from the Midline: On the whole, such a tumor does not readily cause a block of the foramen of Monro; usually, therefore, both lateral ventricles and the third ventricle are visualized. However, if the tumor is far back in the motor area or is large or infiltrating, with great edema of the brain,

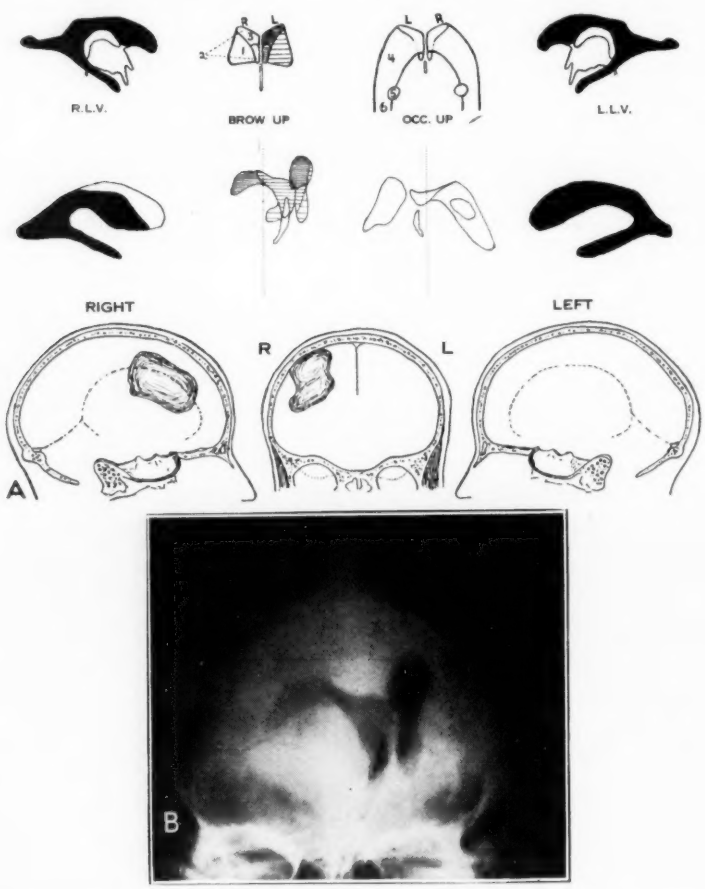


Fig. 6.—(*A*) Tumor of the upper posterior portion of the frontal lobe, lying away from the midline, and (*B*) anteroposterior film used in making the tracing shown in *A*.

the ipsilateral ventricle may not be shown. Almost always there is flattening of portion 3 or a curved "cut-out" of varying pattern as seen laterally. The third ventricle is oblique—following the shift of the ventricular system to the opposite side. Being firmly anchored below, this portion remains central. The contralateral ventricle is dilated. In

encephalographic films the sulcus corporis callosi occasionally adds certain evidence to the lateralization of the tumor. It is our opinion that most of the pressure produced by a tumor in this location is dissipated along the lateral edge and roof of the corpus callosum.

Occasionally a cyst communicates with a ventricle; when this occurs the ventricle again resumes a more normal appearance.

CASE 3 (Mr. O. B., aged 33; fig. 6 *A*).—The left lateral ventricle is moderately dilated and displaced to the left anteriorly. Portion 1 of the right lateral ventricle is almost obliterated from above, and portion 2 is depressed and displaced to the left. This deformity is particularly striking when the relative shape and position of the lateral ventricles are considered, as shown in the analysis. Portions 4 and

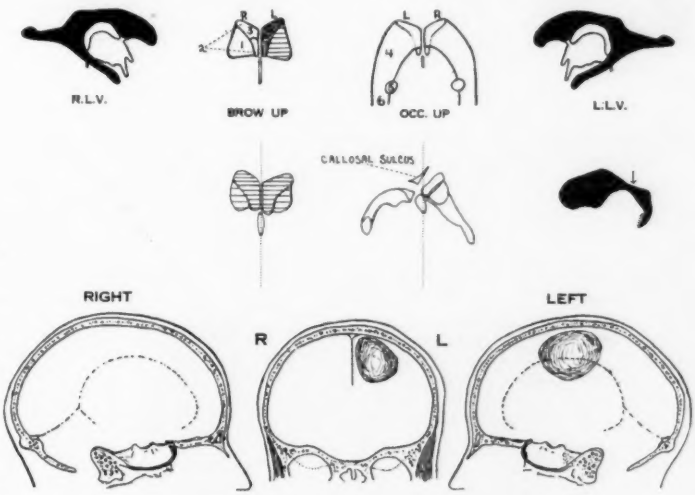


Fig. 7.—Tumor of the upper posterior portion of the frontal lobe, lying away from the midline. The deformity of the callosal sulcus is evident.

5 are not remarkable, but portion 6 is somewhat flattened from above. The third ventricle is slightly dilated and displaced to the left. It is strikingly concave toward the tumor. The tracing of the ventricles with the brow up was made from the roentgenogram reproduced in figure 6 *B*.

CASE 4 (a boy, J. P. B., aged 9 years; fig. 7).—Portions 1 and 2 of the lateral ventricles are symmetrical and only slightly dilated. Portion 3 of the left lateral ventricle is compressed from above. The callosal sulcus, as seen in the view with the occiput up, is obliquely tipped, with its left side considerably lower than its right. The third ventricle is in the midline and is not grossly dilated.

CASE 5 (G. C., a boy aged 15 years; fig. 8 *A*).—The right lateral ventricle is dilated and displaced to the right. Portions 1, 2 and 3 of the left lateral ventricle are depressed and markedly compressed from above. They are also displaced to the right. Portion 6 is distinctly flattened. The third ventricle is concave

toward the tumor and displaced to the right. A reproduction of the original roentgenogram with the brow up is submitted (fig. 8 *B*).

C. Tumors of the Tip of the Frontal Pole: A tumor placed well in front of one anterior horn will result in pressure on portions 1 and 2; if the tumor is large it probably will also collapse portion 3, or most

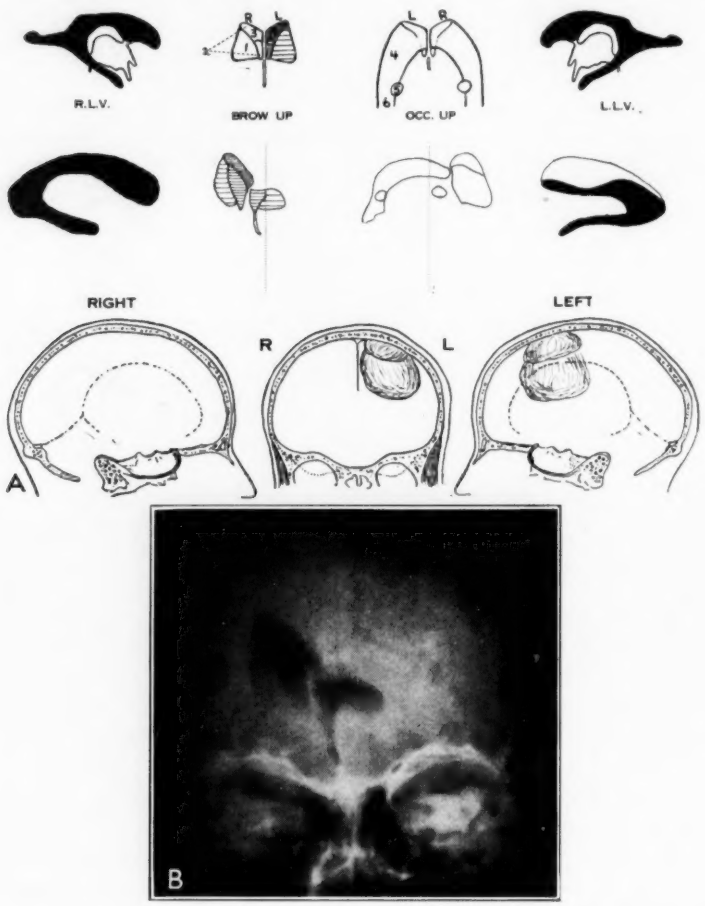


Fig. 8.—(*A*) Tumor of the upper posterior portion of the frontal lobe, lying away from the midline, and (*B*) roentgenogram used in making the tracing shown in *A*.

of it. This distortion results in shifting of the ventricular system to the opposite side, with some obliquity of the third ventricle. If the tumor is bilateral it will deform the lateral ventricle on the other side, with various distortions of the third ventricle.

CASE 6 (Mr. J. M., aged 26; fig. 9).—The left lateral ventricle is uniformly dilated and displaced to the left. Portions 1 and 2 and the anterior part of portion 3 of the right lateral ventricle are flattened from above and displaced to the left. There is some flattening of portion 6. The third ventricle is swung to the left and dilated.

D. Tumors at the Base of the Frontal Lobe and on the Floor of the Anterior Fossa:

A tumor in this region, depending on its size and rapidity of growth, usually lifts portions 1, 2 and 3. We studied a case of a slowly growing meningeal fibroblastoma which caused no evident displacement. Depending on the mesial or the lateral position of the tumor, the ventricle is

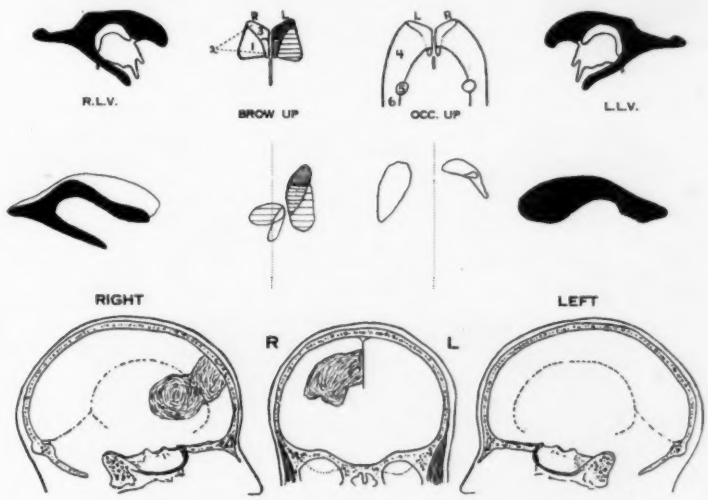


Fig. 9.—Tumor of the tip of the frontal pole.

lifted evenly, or only its lateral edge is elevated. In many cases the distance between the anterior and the temporal horn is increased, as viewed in lateral stereoscopic films. In these instances the temporal horn is flattened or bent downward. This, no doubt, is due to the pressure exerted by the edematous brain as it is squeezed over the posterior edge of the anterior fossa. Associated with these findings there is always dislocation of the ventricular system across the midline, with oblique shifting of the third ventricle, which is usually visible.

CASE 7 (Mr. J. G. E., aged 43; fig. 10 *A*).—The right lateral ventricle is symmetrically dilated. Both lateral ventricles are displaced to the right. Portions 1 and 2 of the left lateral ventricle are flattened from below and present a curved "cut-out" inferiorly and anteriorly. The septum pellucidum and the third ventricle

are displaced to the right, and the third ventricle is dilated. The deformity as seen in the lateral view with the brow up is shown in figure 10 *B*.

E. Tumors Immediately Above the Fissure of Sylvius: Such a tumor tends to displace the third ventricle obliquely toward the opposite side, with a concave surface facing the tumor. It is almost always

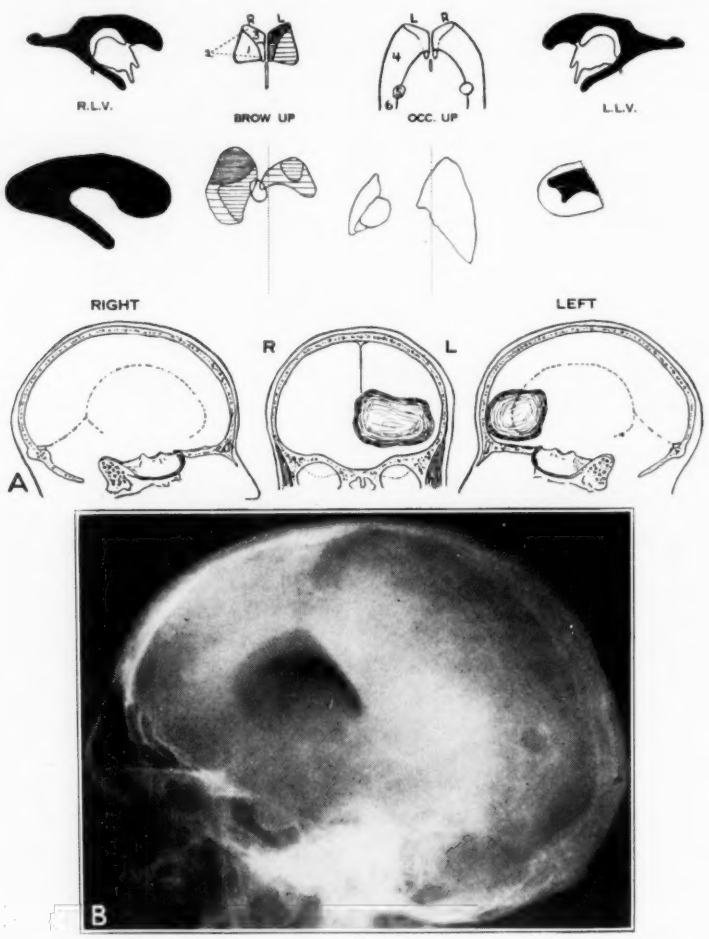


Fig. 10.—(*A*) Tumor situated at the base of the frontal lobe and on the floor of the anterior fossa and (*B*) lateral roentgenogram used in the tracing shown in *A*.

visible, in contradistinction to the tumor of the temporal lobe. A tumor above the Sylvian fissure shifts the ventricular system across the midline and dilates the contralateral ventricle. The ipsilateral ventricle is almost always shown (in 80 per cent of the cases). In two cases, both of

infiltrating tumor, the ventricle on the side of the tumor was not visualized. Almost universally portion 3 is flattened or distorted, and portion 2 is compressed. This is logical when one considers that in most instances the pressure is exerted against the corpus callosum, sometimes lifting and sometimes depressing it.

CASE 8 (Mrs. N. A. H., aged 60; fig. 11).—The right lateral ventricle is generally dilated and displaced to the right. Portions 1 and 2 and part of portion 3 of the left lateral ventricle are compressed, both from side to side and from above. They are displaced to the right with the third ventricle, which is small. The drainage is not complete enough to visualize portion 6 on the left side.

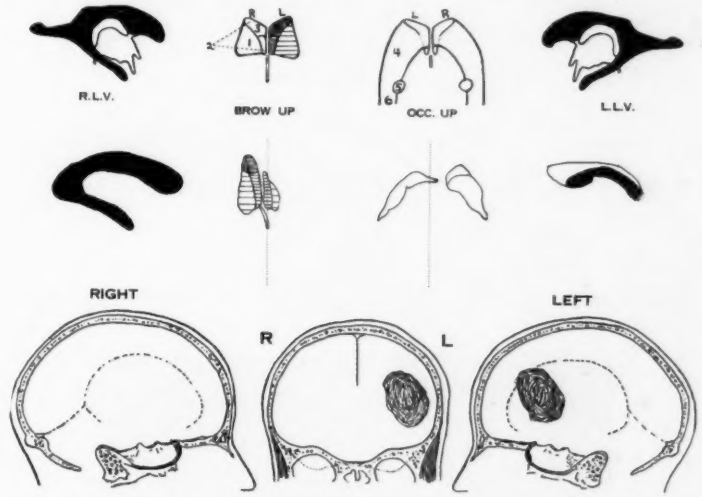


Fig. 11.—Tumor of the frontal lobe immediately above the fissure of Sylvius.

F. Tumors Communicating with the Third Ventricle: These tumors cause a variety of deformities with no definite pattern, depending on the size of the tumor and the amount of involvement of the surrounding structures and the third ventricle.

The third ventricle may be almost obliterated, only a bubble or two of air indicating its presence. The lateral ventricles are sometimes separated widely and distorted. The third ventricle may appear as a thin shadow, with a dilated lateral ventricle, as in the example we show.

CASE 9 (Miss M. K., aged 21; fig. 12 *A*).—The left lateral ventricle is greatly dilated. Portions 1 and 2 of the right lateral ventricle are slightly dilated but much smaller than the corresponding portions of the left lateral ventricle. They are displaced posteriorly and upward. The third ventricle is flattened from side to side and in the midline. The film reproduced in figure 12 *B* shows the relative size and position of the anterior portions of the lateral ventricles as viewed laterally.

Deformities of portions 1, 2 and 3 of the ipsilateral ventricle constitute the most important findings in cases of tumor of the frontal lobe. Alteration in the form or position of one or more of these portions will frequently indicate the exact location of an adjacent tumor. In this respect, we stress the fact that the lateral view with the brow up

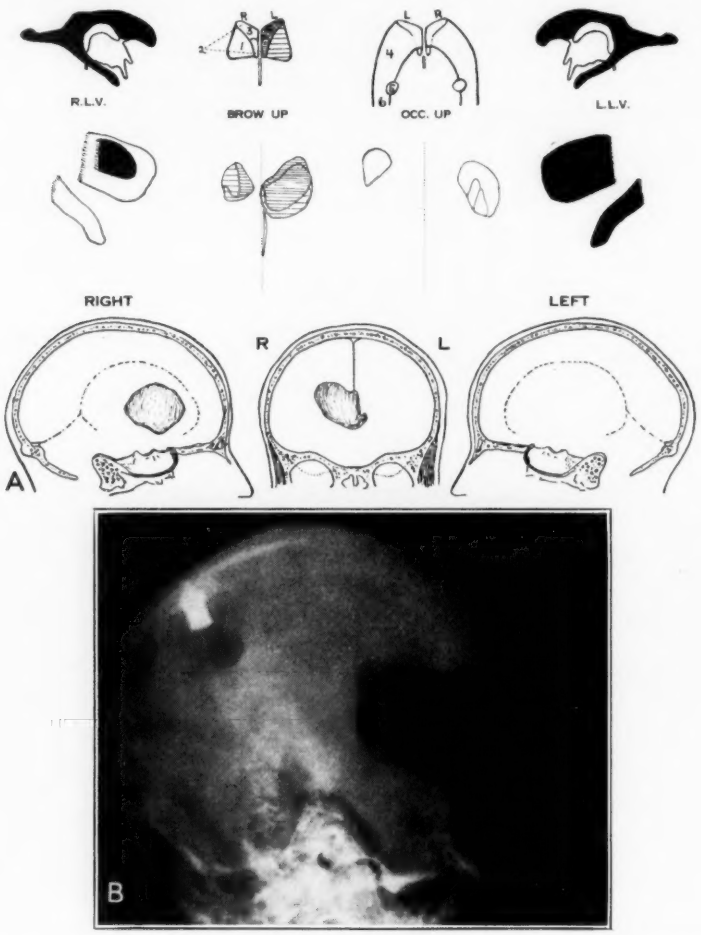


Fig. 12.—(*A*) Tumor of the frontal lobe extending into the third ventricle and (*B*) lateral roentgenogram with the brow up, illustrating the deformity shown in *A*.

will often differentiate between actual deformity and incomplete drainage. Depending on the size and location of the tumor, these portions of the ventricle may be displaced in any direction, or they may be generally or locally compressed. In common with tumors elsewhere in the cerebral

hemispheres, the contralateral ventricle is usually dilated. The third ventricle is visualized in a high percentage of cases but is rather infrequently dilated. A tumor near the temporal lobe and a large tumor farther away may cause uniform compression of portion 6 of the ipsilateral ventricle. The contralateral ventricle and the third ventricle are usually displaced away from the tumor.

Tumors of the Temporal Lobe.—A tumor in the region of the temporal lobe tends to shift the ventricular system across the midline unless it is small or on the base of the middle fossa. Then the septum pellucidum remains almost central. Because the third ventricle is horizontally on a level with the superior and the upper part of the middle temporal gyrus, it is almost always displaced to the opposite side, with its concavity toward the tumor. This is no doubt due to the pressure of the thalamus against it. The third ventricle often is not seen, but when visible it is frequently dilated, owing to indirect pressure on the aqueduct of Sylvius. When the contralateral ventricle only is visible, it is probable that the thalamus is forced against the interventricular foramina, as this occurs most frequently in cases of a large infiltrating tumor of the posterior part of the temporal lobe.

In cases of tumor of the temporal lobe deformities of portion 6 are of greatest diagnostic value. Valuable evidence is obtained from failure to fill portion 6 in spite of careful posturing, particularly if the corresponding portion of the opposite ventricle is normal in shape and position. Lateral stereoscopic films and postero-anterior films with the brow down are the most helpful.

In many cases portion 6 is lifted, depressed, flattened, displaced medially, twisted, bent at a sharp angle or absent; each of these distortions is seen in this series. An infiltrating tumor appears to damage rapidly the inferior horn, so that its filling is irregular or possible only in its posterior portion. Anatomically, we believe that portion 6 is constantly regular in its shape and position.

It seems to be an almost universal finding that portions 1 and 2 of the contralateral ventricle are dilated out of proportion to the rest of the ventricle. This was true in fourteen of nineteen cases in this series.

As already mentioned, a tumor of the temporal lobe situated entirely within this lobe may cause depression of the ipsilateral ventricle. Knowledge of this phenomenon is important, as otherwise the diagnosis of a lesion of the frontal lobe will be made.

CASE 10 (Mrs. M. C., aged 51; fig. 13).—The left lateral ventricle is distinctly enlarged and displaced slightly to the left. The right lateral ventricle is also enlarged, but not so markedly. Portion 6 of this ventricle is smaller than that

of the left lateral ventricle and is definitely elevated and slightly shortened. The third ventricle is dilated and displaced to the left.

Case 11 (M. R., a boy aged 7 years; fig. 14).—The right lateral ventricle is moderately dilated and displaced to the right. The left lateral ventricle is almost

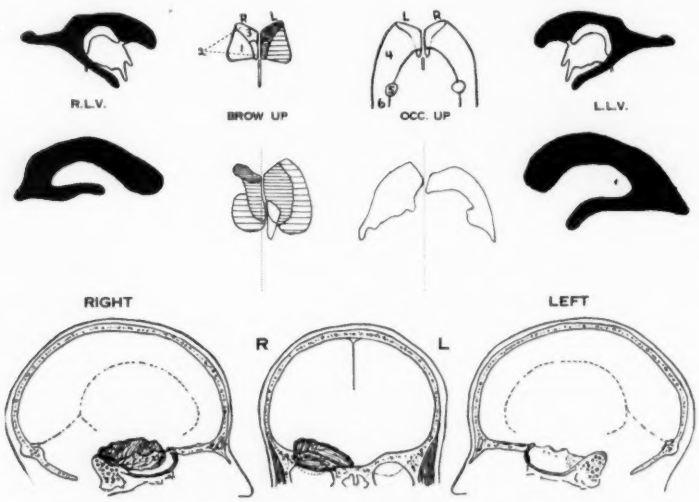


Fig. 13.—Tumor of the temporal lobe elevating portion 6.

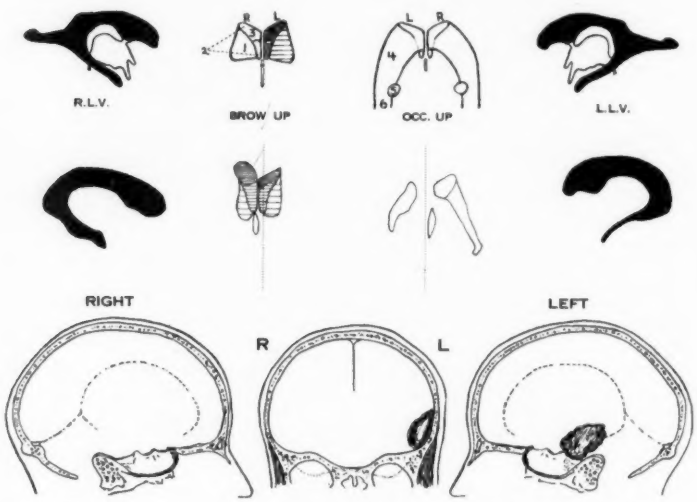


Fig. 14.—Tumor of the temporal lobe flattening portion 6.

normal in size anteriorly but is displaced to the right. Portion 6 is much flattened as seen in the lateral view and is less extensive than its fellow as seen in the view with the occiput up. The third ventricle is only slightly dilated but is displaced to the right as visualized both anteriorly and posteriorly.

CASE 12 (Mrs. A. J.; fig. 15 *A*).—The left lateral ventricle is dilated. This is most marked in portion 1. Portions 2 and 3 are carried to the left. The right lateral ventricle is depressed in portions 1 and 3 and presumably in portion 2. Portion 6 is much thinned as viewed laterally and is displaced medially as shown in the view with the brow up.

Portion 6 of the left lateral ventricle contains trapped gas and is also visible in the view with the brow up. Its position is normal and evidently different from

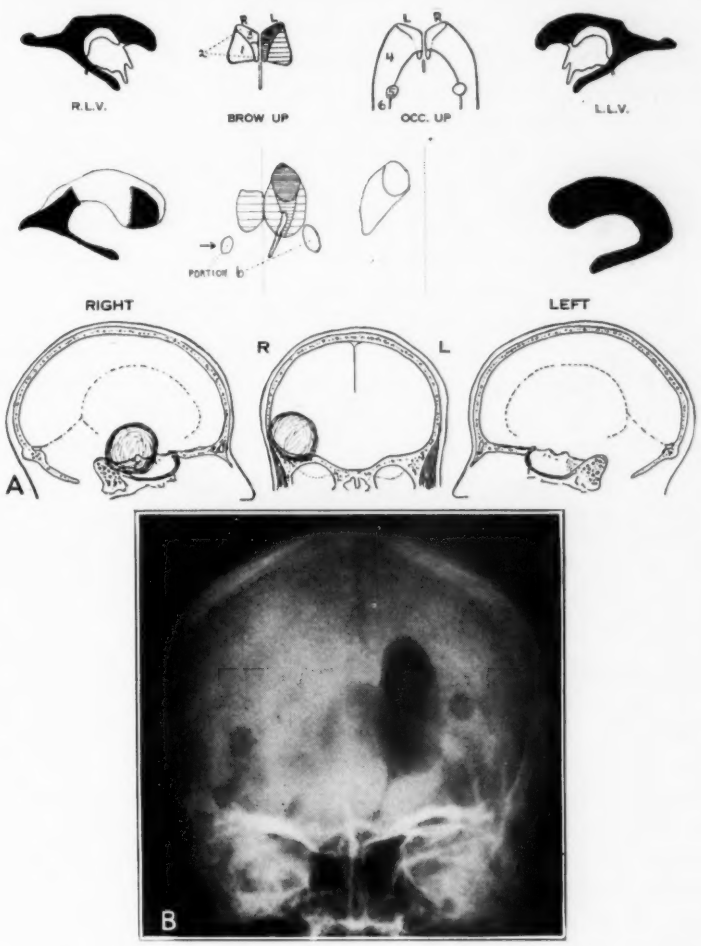


Fig. 15.—(*A*) Tumor of the temporal lobe displacing portion 6 medially and depressing the ipsilateral ventricle and (*B*) anteroposterior roentgenogram showing medially displaced portion 6, as well as the other ventricular deformities illustrated in the tracing with the brow up shown in *A*.

the displaced portion 6 of the right lateral ventricle. The original film is reproduced to show this deformity (fig. 15 *B*). The third ventricle is swung away from the tumor and is somewhat concave toward it.

The tumor is entirely within the temporal lobe, and this case illustrates well the depression of the ipsilateral ventricle with a tumor of the temporal lobe.

Deformities and displacements of portion 6 of the ipsilateral ventricle are the most important findings in cases of tumor of the temporal lobe. There is usually displacement of the ventricular system across the midline, away from the tumor. The third ventricle commonly is not filled but when visible is often concave toward the lesion. Not infrequently the ipsilateral ventricle is depressed, probably owing to its slipping downward under the free edge of the falx.

Tumors of the Parietal Lobe.—A tumor located in the parietal lobe usually displaces the ventricular system across the midline. The contralateral ventricle is dilated. The third ventricle is oblique but not as concave as in a case of tumor of the temporal lobe. It was visualized in every case in this series. Portion 3 of the ipsilateral ventricle is flattened or almost obliterated. If the tumor presses down over a wide area, portion 3 appears as a thin, dense strip of air.

A huge, space-occupying tumor, an infiltrating tumor with edema or a tumor in which a sudden hemorrhage occurs may cause occlusion of the interventricular foramen, so that the air cannot fill the ipsilateral ventricle.

Lateral films usually show a filling defect on the superior surface of portions 3 and 4. This occurs with a tumor located well up on the side of the hemisphere.

Tumors of the posterior part of the parietal region may force the ipsilateral ventricle forward, so that comparative measurements of the distance between the anterior ends of portion 1 and the frontal bone may prove of value. True lateral films are essential.

The callosal sulcus may indicate the hemisphere involved, as in two cases of this group it was found to be depressed on the side of the tumor.

In a number of cases flattening of portion 6 (the temporal horn) was evident; as one would expect, this occurs with a large tumor or when the tumor also enters the confines of the temporal lobe. The absence of portion 5 is of little diagnostic value, even if the corresponding portion of the opposite ventricle is filled.[4]

Tumors of the Parietal Lobe Lying at the Midline: Such a tumor, being situated above portion 4, separates these areas as seen in postero-anterior films, with flattening of portion 4 on the side of the tumor. Because the greatest pressure is exerted at the junction of portion 3 with portion 4, portion 3 often appears in lateral films as an elongated sickle-like strip of air.

4. Penfield, Wilder G.: Cerebral Pneumography: Its Dangers and Uses, Arch. Neurol. & Psychiat. **13**:580-591 (May) 1925.

A tumor of the falx in the parietal region acts similarly to a tumor of the falx in the frontal area and impinges against the contralateral ventricle; thus, portion 3, as well as part of portion 2, is carried laterally.

CASE 13 (Dr. J. W., aged 60; fig. 16).—The lateral ventricle is markedly displaced to the left and dilated. Portions 1 and 2 of the right lateral ventricle are comparatively normal in size and shape but are displaced to the left. Portion 3 is depressed and much compressed posteriorly, so that it is sickle shaped. It is concave superiorly as seen in the anteroposterior view. The remainder of the ventricle cannot be visualized. The third ventricle is displaced to the left, following the lateral ventricles, but it is not dilated.

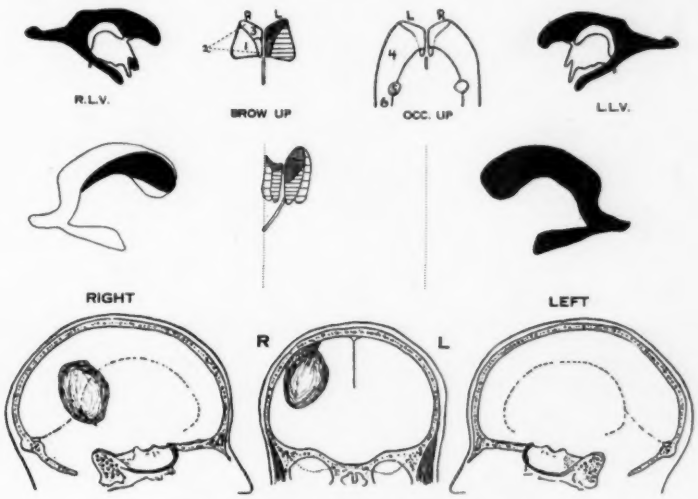


Fig. 16.—Tumor of the parietal lobe.

CASE 14 (Mr. C. L., aged 36; fig. 17 *A*).—Both lateral ventricles are displaced to the left. The left lateral ventricle is not otherwise grossly abnormal. Portion 1 of the right lateral ventricle is of normal size and shape. Portions 2, 3 and 4 are markedly compressed from above and are also depressed. The third ventricle is moderately dilated and displaced to the left. The roentgenograms reproduced in figures 17 *B* and *C* were used to make a composite view illustrating almost the entire right lateral ventricle and the anterior portion of the left lateral ventricle.

This deformity closely simulates that seen with a tumor of the frontal lobe close to the midline, but it involves the lateral ventricle farther posteriorly and has not encroached on portion 1.

CASE 15 (Miss R. S., aged 18; fig. 18).—The left lateral ventricle is not dilated but is displaced to the left. Portion 1 of the right lateral ventricle is also displaced to the left but otherwise is not greatly affected. Portions 2 and 3 are compressed from above, and portion 3 is markedly depressed and displaced forward. Portion 4 is seen in the view with the occiput up and is also depressed. The third ventricle is displaced to the left and is slightly concave to the right. It is not dilated.

A tumor situated in the parietal lobe commonly deforms and displaces portions 3 and 4 of the ipsilateral ventricle. Portions 2 and 6 are frequently less markedly deformed. Ventricular shift to the side away from the tumor is the rule, and moderate dilatation of the contralateral ventricle occurs in 75 per cent of the cases. The third ventricle is uniformly visualized and commonly oblique but is usually neither

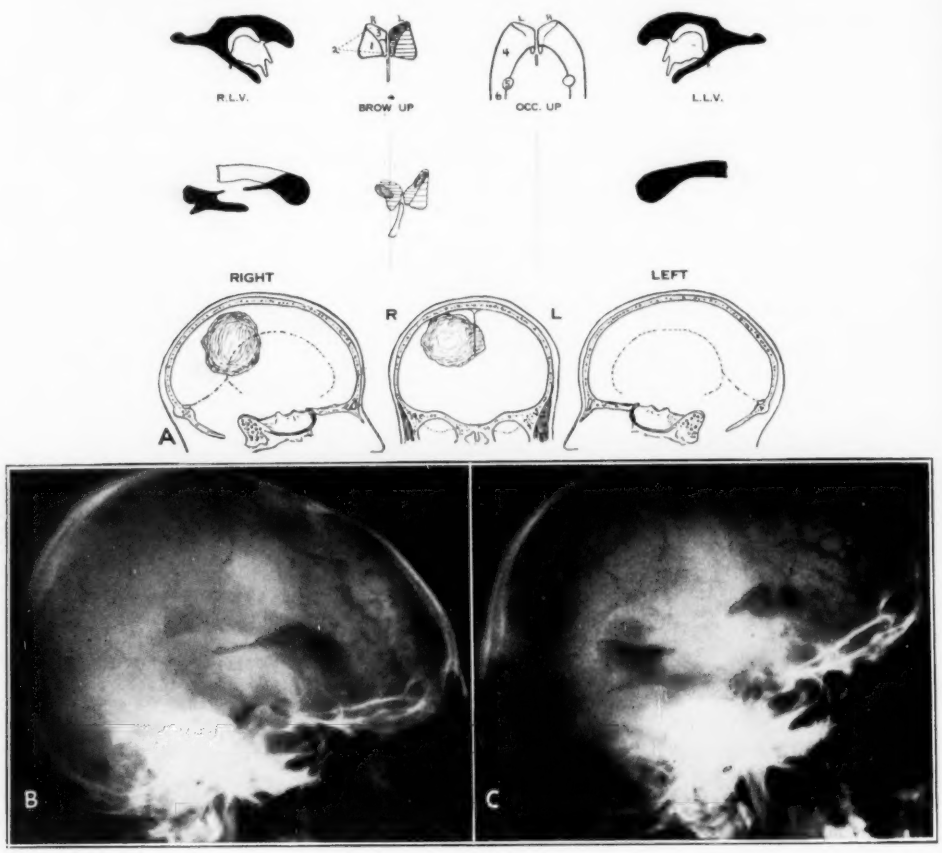


Fig. 17.—(*A*) Tumor of the parietal lobe extending across the midline, and (*B*) one of the roentgenograms used in making the tracing shown in *A* and (*C*) second roentgenogram used in making the same tracing.

markedly dilated nor concave toward the tumor. This lack of concavity and less marked dilatation constitute a distinct difference from the deformity noted with tumor of the temporal lobe.

Tumors of the Occipital Lobe.—When of considerable size or associated with a hemorrhage, a tumor of the occipital lobe displaces the

ventricular system much as does one of the posterior parts of the parietal lobe, for it exerts most of its force against the posterior part of the corpus callosum. This compresses portions 3 and 4. It also tends to push the ventricular system to the opposite side and forward. Measurements of the distance between the tip of the anterior horn and the frontal bone, as well as the base of the anterior fossa, may be of value.

Portion 5 (the posterior horn) may not fill at all, and the lateral film shows almost a vertical plane at the posterior limit of portion 4. Here, again, one must take into consideration the frequent anatomic variation of this area.

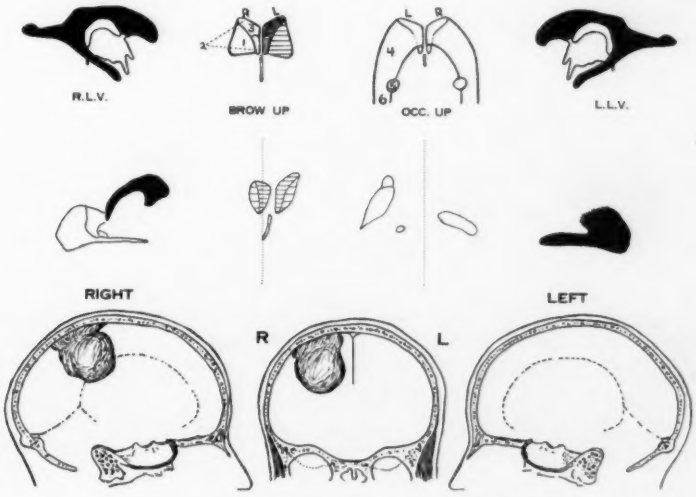


Fig. 18.—Tumor of the parietal lobe.

The opposite ventricle is usually dilated. The opposite posterior horn is usually not altered, probably because of the strength and width of the falx, as pointed out by Dandy,[5] but also, we think, because of the distance of the horn from the falx.

The third ventricle is constantly visible.

In two of the cases there was complete absence of gas in the lateral ventricle on the side of the tumor, though the third ventricle was visible and slightly convex toward the ipsilateral side. It is reasonable to assume that the oblique dislocation of the ventricular system results in serious interference with the patency of the interventricular foramen of the side of the tumor.

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5. Dandy, Walter E., in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12.

CASE 16 (Mr. G. L., aged 32; fig. 19).—The right lateral ventricle is dilated and displaced to the right. The left lateral ventricle is also moderately dilated and displaced to the right. It is somewhat depressed in portions 1 and 2. Portion 3 is not visualized, owing to incomplete filling. Portion 4 is displaced anteriorly and is compressed from behind to a moderate extent. Portion 6 is also moderately compressed. Portion 5 is either undeveloped or obliterated. The third ventricle is slightly dilated and displaced to the right, following the lateral ventricles.

The maximum deformity caused by a tumor of the occipital lobe involves portion 4, probably owing to general increase of the volume of the brain on the side of the lesion. In spite of the posterior position of the tumor, the lateral ventricles commonly migrate to the opposite

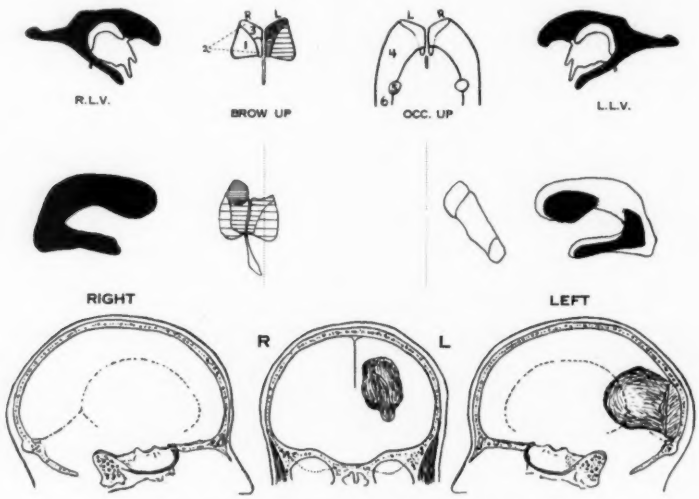

Fig. 19.—Tumor of the occipital lobe.

side even anteriorly, and the third ventricle follows them. The third ventricle is constantly visible, but the ipsilateral ventricle is less frequently demonstrated.

SUMMARY

In this first report of a pneumographic study of one hundred and twenty cases of tumor of the brain in which the diagnosis was verified, there are included cases of tumor involving the lobes of the cerebrum.

We describe a form which we have used and which we believe presents an exact and concise picture in each case from the standpoint of a pneumographic analysis.

In the light of present knowledge and from the interpretation of these cases it is our opinion that a locational diagnosis of a tumor of a hemisphere can be made in nearly every case on the basis of a study of the films alone.

This analysis includes only true tumors of the brain, but it must be borne in mind that any expanding lesion, such as a hemorrhage, abscess or cyst, may produce similar deformities.

CONCLUSIONS

If in true anteroposterior films the ventricular system is seen to have migrated appreciably to either side of the midline, one has good reason to make a diagnosis of tumor on the side opposite the migration (cerebral atrophy having been excluded).

If there is a deformity, "cut-out" or filling defect in any part of the lateral ventricles and, certainly, if this persists in spite of adequate posturing, a diagnosis of tumor in this locality should be made, provided that a brain scar can be ruled out. This does not apply to portion 5 (the posterior horn), as it has been repeatedly shown by Penfield and others that the posterior horn varies greatly in size and shape and may often be absent.

If there is hydrocephalus of one lateral ventricle, possibly associated with dilatation of the third ventricle, a tumor of the opposite hemisphere is indicated (cerebral atrophy having been excluded).

If there is a definite forward dislocation of either one or both lateral ventricles as seen in true lateral films, a tumor of the brain is present, usually located in the postparietal or occipital region.

If in true anteroposterior films the third ventricle is obliquely shifted to either side or is definitely concave to either side, a tumor is present in the hemisphere away from the shift or concavity.

If there is unmistakable displacement of one of the constant sulci, such as the callosal sulcus, or complete absence of the subarachnoid channels over an area, the other channels being filled in a normal manner, the diagnosis of a tumor of the brain should receive serious consideration.

PNEUMOGRAPHIC LOCALIZATION OF TUMORS OF THE BRAIN

II. TUMORS INVOLVING THE BASAL GANGLIA, LATERAL VENTRICLES, BRAIN STEM AND CEREBELLUM

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AND
ARTHUR E. CHILDE, M.D.
MONTREAL, CANADA

In a previous communication [1] we analyzed the pneumographic findings in cases of tumor of the brain involving the lobes of the cerebrum and outlined a form which we have used in their study. The present paper analyzes the findings in the remainder of the one hundred and twenty cases in which the diagnosis of tumor was verified. It includes the cases of tumor involving the basal ganglia, lateral ventricles, brain stem and cerebellum.

TUMORS OF THE POSTERIOR FOSSA

A tumor of the posterior fossa causes the greatest degree of hydrocephalus. It dilates all parts of the ventricular system above the block. This dilatation is seen to be symmetrical, when the ventricular system is satisfactorily drained. The lateral ventricles are round in all portions, and the third ventricle is greatly dilated. In this part of the system no constant factor has been found that is of value in determining the side of the cerebellum involved by the tumor. In disagreement with the original statement of Elsberg and Silbert,[2] we do not find the posterior horns altered in any regular way. Moreover, as shown by Penfield and others, the posterior horns vary greatly, sometimes being absent, so that they cannot be used as a diagnostic index.

From the Montreal Neurological Institute, McGill University.

The original report of this study was read at the meeting of the Neurological Section of the Montreal Medico-Chirurgical Society at Montreal, Canada, April 17, 1935.

1. McConnell, Lorne H., and Childe, Arthur E.: Pneumographic Localization of Tumors of the Brain: I. Tumors of the Lobes of the Cerebrum, Arch. Neurol. & Psychiat. this issue, p. 33.

2. Elsberg, C. A., and Silbert, S.: The Ventricular System: Its Relation to the Cerebellum; Ventriculography and Other Ventricular Evidence in the Recognition of Cerebellar Disease, Arch. Neurol. & Psychiat. **19**:596-616 (April) 1928.

One of us (L. H. M.) draws attention to the fact that in seven of the twenty-two cases used the side of the tumor was definitely shown by the curve of the aqueduct of Sylvius as it was pushed laterally by the tumor, as seen in anteroposterior or postero-anterior films. A separate study of these cases demonstrates that during the posturing certain maneuvers must have occurred to allow free passage of the gas into the aqueduct. Since one can usually best see the aqueduct and the upper part of the fourth ventricle when viewed laterally, it appears as a proper conclusion that if lateral films in which gas is shown in the aqueduct are immediately developed and then, without moving the patient, an anteroposterior and a postero-anterior film are taken, one should see the aqueduct. From this study it was found that the gas entered the aqueduct of Sylvius when the side of the tumor was down against the film, with the aqueduct, of course, at a higher level than the rest of the ventricular system. Further work on posturing in cases of tumor of the posterior fossa will, no doubt, develop a technic which insures the demonstration of the aqueduct of Sylvius in a much higher percentage of cases.

Occasionally the upper part of the fourth ventricle was visualized, showing a definite "cut-out."

CASE 1 (Mrs. M. K., aged 47; fig. 1 *A*).—Both lateral ventricles and the third ventricle are symmetrically dilated. The views both with the brow up and with the occiput up show the aqueduct of Sylvius to be displaced to the left and concave on the side toward the tumor, which involved the right eighth nerve.

In the film taken with the occiput up (fig. 1 *B*) the displacement of the aqueduct is clearly visible.

CASE 2 (Mrs. R. K., aged 26; fig. 2).—Both lateral ventricles are symmetrically dilated. The third ventricle is dilated and in the midline. The aqueduct of Sylvius and the upper portion of the fourth ventricle are shown in the lateral views with the right side up; in the views with the brow up and with the occiput up they are seen to be displaced to the right, away from the tumor.

CASE 3 (Mr. C. L., aged 41; fig. 3).—Both lateral ventricles are symmetrically dilated. The third ventricle is also greatly dilated. The aqueduct of Sylvius is visible and is not dilated. It is displaced slightly but definitely forward, suggesting pressure near the midline and posterior to this structure.

CASE 4 (C. C., a boy aged 12 years; fig. 4).—There is marked dilatation of both lateral ventricles. The third ventricle and the aqueduct of Sylvius are also dilated and are in the midline. A V-shaped filling defect involves the fourth ventricle and obliterates all but its upper portion, as shown in the view with the occiput up.

A tumor of the posterior fossa causes dilatation of the ventricular system above the block. Thus, the third ventricle can be readily shown and not infrequently the aqueduct and even the upper part of the fourth ventricle. Displacements and deformities of the last-mentioned structures may localize the lesion.

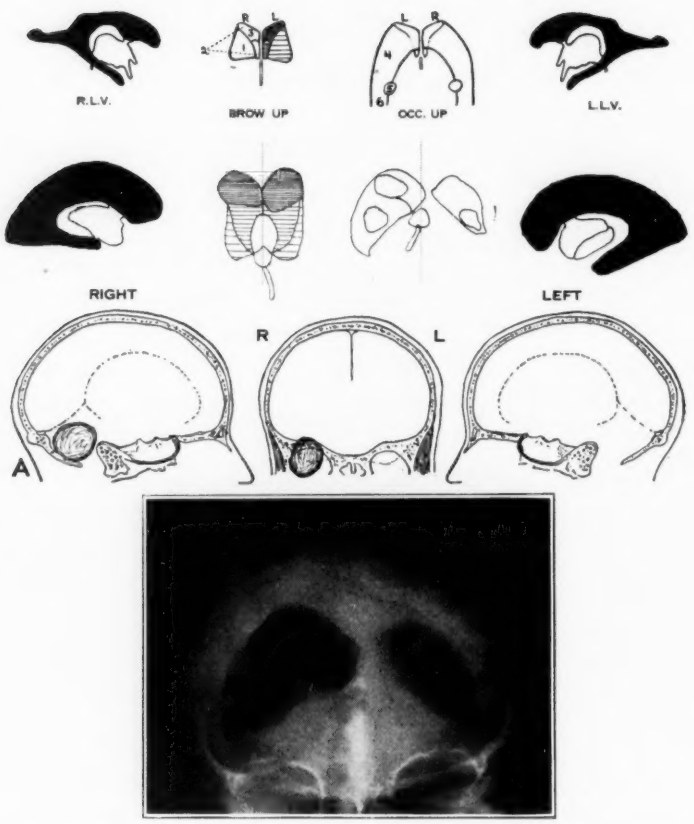

Fig. 1.—*A*, tumor of the posterior fossa causing lateral displacement of the aqueduct of Sylvius and *B*, postero-anterior roentgenogram used in making the tracings shown in *A*.

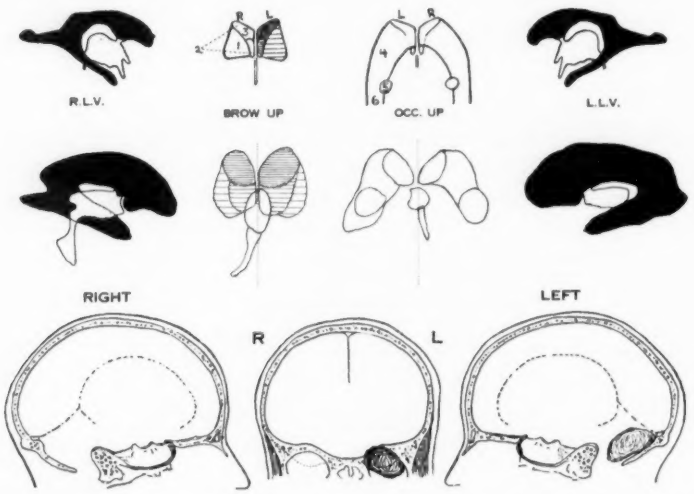

Fig. 2.—Tumor of the posterior fossa causing lateral displacement of the aqueduct of Sylvius.

MULTIPLE TUMORS OF THE BRAIN

When a number of tumors occur in the brain, any variety of filling defect or shift of the system may occur, depending on the shape or size of the neoplasm. When one tumor is much larger than any of the

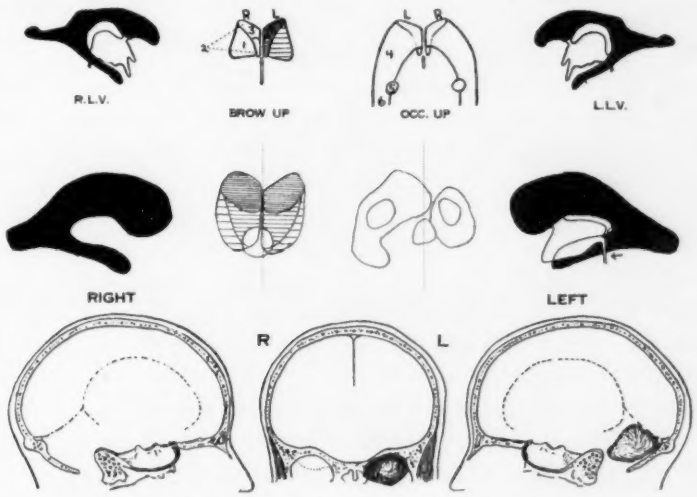

Fig. 3.—Tumor of the posterior fossa causing anterior displacement of the aqueduct of Sylvius.

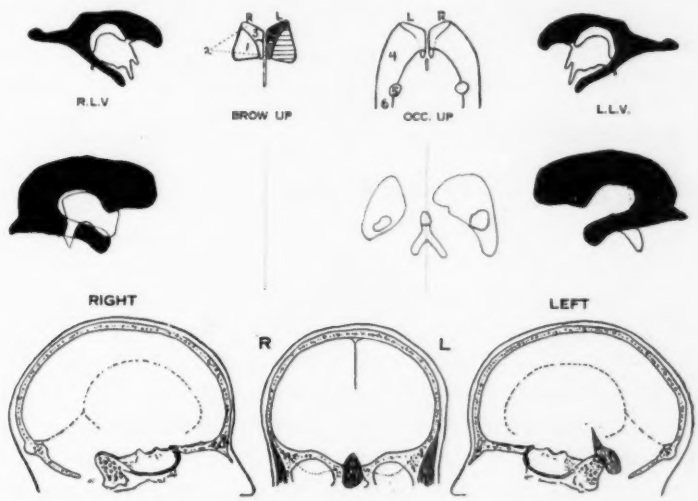

Fig. 4.—Tumor of the posterior fossa producing a filling defect in the fourth ventricle.

others, the pressure effect of this lesion will probably determine the distortion shown in the films. If a number of small tumors invade the brain more or less equally on the two sides, there is usually no shift of

the ventricular system, and unless there is a filling defect, one would probably fail to make a diagnosis from the films. On the other hand, a comparatively small tumor located in a strategic position, for example, near the aqueduct, may by producing hydrocephalus overshadow the effect of a much larger lesion.

TUMORS OF THE LATERAL VENTRICLE

Only two tumors of the lateral ventricle are included in this series. When gas enters the opposite ventricle it fills the ventricular system to the anterior border of the tumor if the tumor is posterior to the interventricular foramen, or to the posterior border if it is in front of the foramen, provided that the tumor tightly occludes the ventricle. By puncturing the opposite ventricle it is possible to fill the space posterior or anterior to the tumor, and then the filling defect of the tumor is shown in bold relief. In one case the air passed around the tumor apparently without difficulty; so one could be sure that the growth did not completely block the ventricle.

Enlargement of the defect in the air shadow normally produced by the choroid plexus, such as sometimes occurs after ventricular puncture, probably owing to hemorrhage, must not be confused with a neoplasm. This shadow has recently been described by Dyke and his associates.[3] Occasionally the outlines of one or both lateral ventricles will be irregular, owing to extension of the tumor from the third ventricle.

CASE 5 (Mrs. O. L., aged 47; fig. 5).—A large filling defect involves portion 4 of the left lateral ventricle. Gas has passed around this, proving that the lumen of the ventricle is not completely occluded. Both lateral ventricles and the third ventricle are symmetrically dilated. This dilatation later proved to be due to a tumor of the posterior fossa.

TUMORS OF THE PITUITARY GLAND

As this study includes but two examples of this type of tumor and as in neither case was the visualization entirely satisfactory, we do not feel qualified to discuss this aspect of pneumographic interpretation.

TUMORS OF THE PONS

In cases in which encephalography is used absence of the cisterna pontis may be of value. Increase of the normal measurement between the floor of the fourth ventricle and the dorsum sellae is significant. Dyke and Davidoff [4] pointed out that in the adult this averages 37 mm.,

3. Dyke, Cornelius G.; Elsberg, Charles A., and Davidoff, Leo M.: Enlargement of the Defect in the Air Shadow Normally Produced by the Choroid Plexus, Am. J. Roentgenol. **33**:736-743 (June) 1935.

4. Dyke, Cornelius G., and Davidoff, Leo M.: The Demonstration of Normal Cerebral Structures by Means of Encephalography: IV. The Subarachnoid Cisterns and Their Contents, Bull. Neurol. Inst. New York **3**:418-445 (March) 1934.

the normal limits being from 33 to 40 mm. When ventriculography is resorted to, "tell-tale bubbles" around the posterior part of the third ventricle may be suggestive. Penfield has frequently pointed out the occurrence of these bubbles around tumors. From the pneumographic standpoint, the differentiation of such a tumor from a tumor of the posterior fossa is important only in saving the patient from a useless operation and the surgeon and operating staff a great deal of time.

CASE 6 (R. M., a youth aged 16; fig. 6).—There is marked symmetrical dilatation of the lateral ventricles. The third ventricle is also dilated and shows in all its extent. The aqueduct of Sylvius is not visualized. There are a number of bubbles of gas around the posterior inferior portion of the third ventricle, as shown in the view with the occiput up.

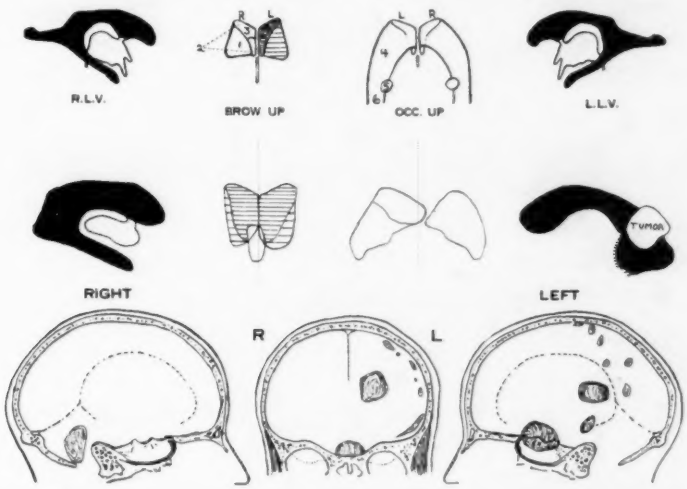

Fig. 5.—Tumor of the lateral ventricle. Multiple tumors in other locations are also present.

TUMORS OF THE THIRD VENTRICLE

Four cases of true tumor of the third ventricle are included in this study. Diagnosis of such a tumor is made without great difficulty when there is a definite filling defect or even when the tumor is large, almost obliterating the third ventricle but producing filling defects in the mesial aspects of the lateral ventricles.

When, however, the third ventricle is not visualized, one is likely to mistrust one's technic of draining the third ventricle and think that the gas has escaped from the third ventricle or has not yet entered it and, because of hydrocephalus, may make a diagnosis of block of the posterior fossa. This reasoning is fallacious, since in block of the posterior fossa when the lateral ventricles are hugely dilated the third

ventricle will also be greatly distended. Consequently, it will be almost impossible not to fill, at least partially, the third ventricle. Therefore, when one sees bilateral hydrocephalus and after proper posturing fails to see the third ventricle in any of its portions, one must believe in one's technic and make a diagnosis of tumor of the third ventricle.

CASE 7 (Mr. G. D., aged 39; fig. 7).—There is tremendous dilatation of the lateral ventricles. A filling defect projects upward and posteriorly into portion 4 of the left lateral ventricle. Corresponding to this there is also a filling defect in the posterior portion of the third ventricle. These defects are conclusively shown in the lateral and postero-anterior views with the occiput up. The aqueduct and the fourth ventricle are not shown.

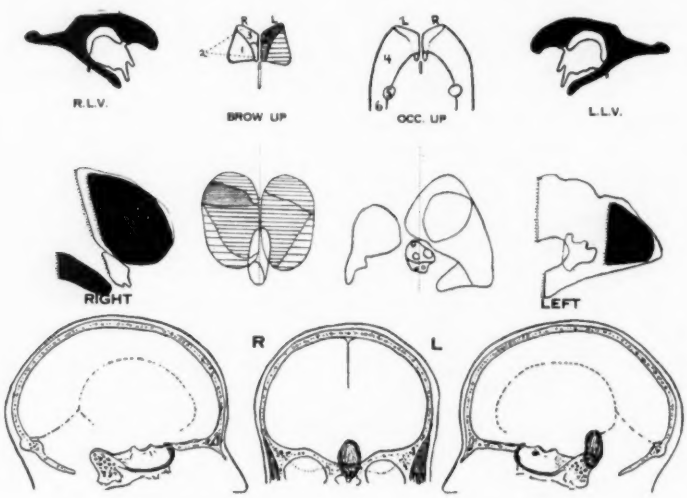

Fig. 6.—Tumor of the pons. Bubbles are shown in the posterior portion of the third ventricle.

CASE 8 (P. M., a youth aged 17; fig. 8).—Both lateral ventricles are symmetrically dilated. The septum pellucidum is in the midline. The third ventricle is not seen, in spite of careful posturing of the head. It is believed that if the lesion were in the posterior fossa it would be almost impossible to keep gas out of the third ventricle, as it also would be generally dilated.

TUMORS OF THE PINEAL GLAND

It is well recognized that a tumor of the pineal gland presents the greatest difficulty in diagnosis from a ventriculographic standpoint, as it may readily be mistaken for a large tumor in the region of the aqueduct of Sylvius.

It is of extreme importance to differentiate a tumor of the pineal body from a tumor of the posterior fossa because of the difference in

the surgical approach. To attempt a suboccipital operation and find that the tumor is one of the pineal gland, or vice versa, is almost certain to be a fatal mistake. A tumor of the pineal gland may be mistaken for

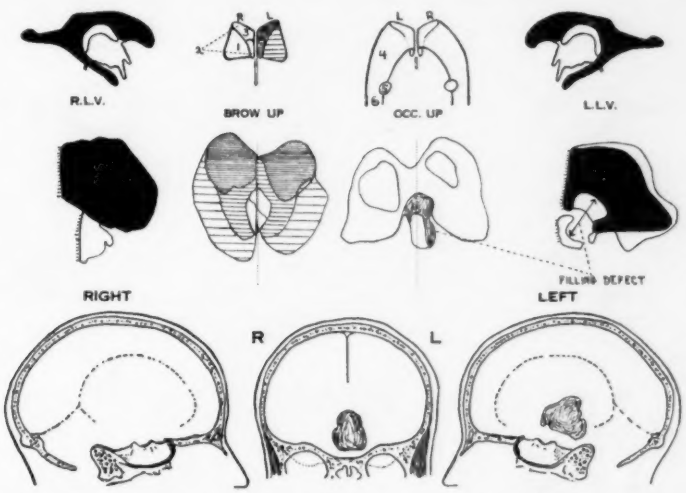

Fig. 7.—Tumor of the third ventricle. A filling defect involves both the third and the left lateral ventricle.

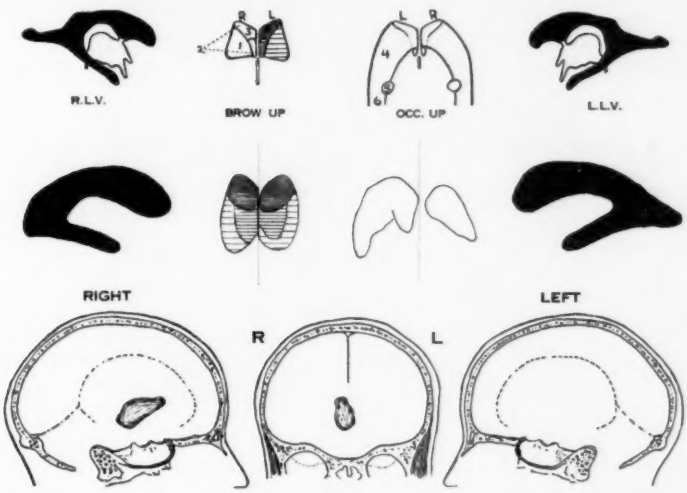

Fig. 8.—Tumor of the third ventricle, with complete obliteration of the ventricle.

one of the posterior part of the third ventricle, but the error is not grave, as the approach for the removal of the tumor is practically the same.

If the tumor is large there is bilateral hydrocephalus, with enlargement of the third ventricle, and, as pointed out by Dandy, the suprapineal recess is either absent or lifted. In one case in this series it was absent, but the upper and posterior part of the third ventricle was sharpened by a "cut-out" and resembled the suprapineal recess.

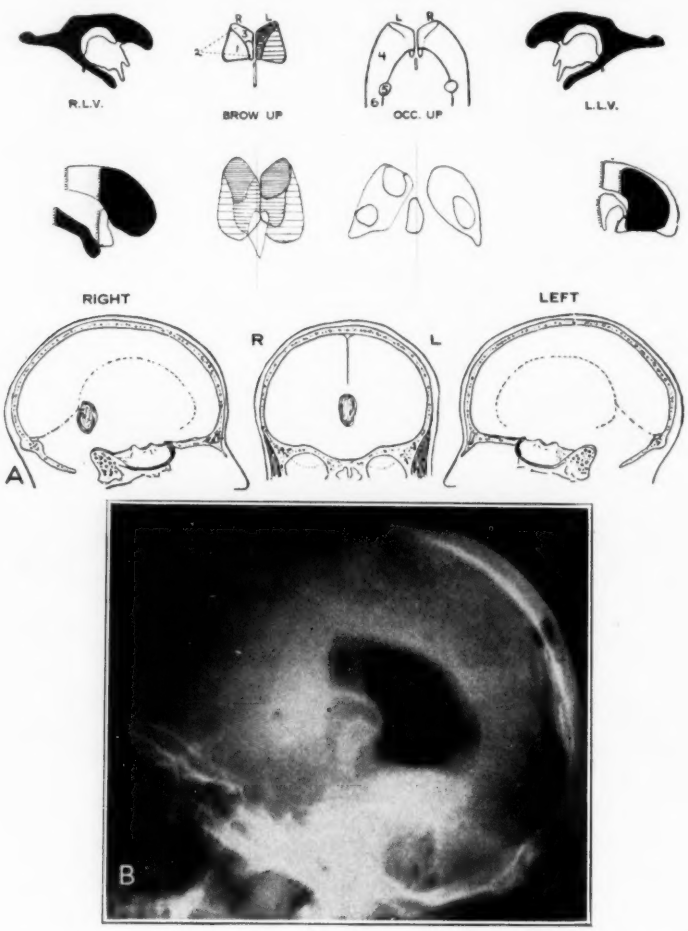

Fig. 9.—(*A*) tumor of the pineal gland and (*B*) lateral roentgenogram (with the brow down), illustrating the deformity of the posterior portion of the third ventricle, as indicated in the tracings shown in *A*.

There is usually a definite filling defect in the posterior part of the third ventricle as the tumor pushes forward.

We find that by careful study of the lateral films taken with the occiput up it is usually possible to see the tumor, because of the filling

defect it causes against the adjacent walls of the lateral ventricles in the region where portion 4 merges into portion 6.

CASE 9 (H. F., a boy aged 13 years; fig. 9 *A*).—There is symmetrical dilatation of both lateral ventricles. The anterior portion of the third ventricle is likewise dilated, but posteriorly there is a large "cut-out." The suprapineal recess is really absent but is simulated by the upward projection of the tumor into the ventricle. It should be added that lateral films with the occiput up were most valuable in this case; one, reproduced in figure 9 *B*, shows the projection of the tumor into the third ventricle posteriorly.

TUMORS OF THE THALAMUS AND BASAL REGION

It was thought wiser to include tumors of the thalamus and basal region under this caption, for usually in cases in which operation is

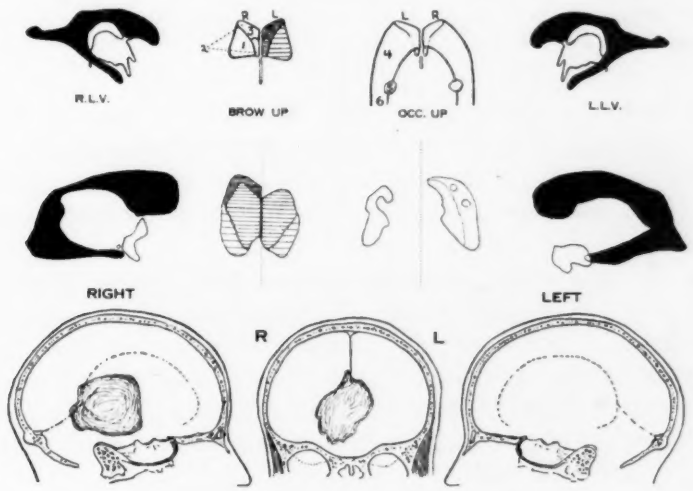

Fig. 10.—Tumor of the thalamus.

performed the tumor has already made inroads from other directions into the thalamus or from the thalamus into surrounding structures. We find that if the thalamus is infiltrated either by the tumor itself or by edema the picture is striking and can hardly be mistaken for any other lesion.

Owing to its expansion the thalamus lifts all of portion 3 and pushes back portion 4. This creates a high-arched curve of the affected lateral ventricle, which shows in bold relief against the opposite ventricle when viewed in lateral films. The elevation of portion 3 is also evident in anteroposterior and postero-anterior views. One is likely to be misled by the filling defect produced in the posterior part of the third ventricle.

This defect is caused by the enlarged thalamus expanding medially, and a tumor of the third ventricle may thus be simulated. The high, even arch of portions 3 and 4, in contradistinction to the normal arch in the contralateral ventricle, could not exist with a tumor of the third ventricle causing complete obliteration of its posterior part and lifting but one lateral ventricle.

In addition, there is usually bilateral hydrocephalus due to pressure on the midbrain and consequent obstruction of the aqueduct of Sylvius.

CASE 10 (Mrs. E. T., aged 52; fig. 10).—Both lateral ventricles are dilated. The dilatation on the left side is symmetrical. Portion 3 of the right lateral ventricle is lifted and compressed, and portion 4 is displaced posteriorly and compressed. The lifting of portion 3 is evident in the view with the brow up and also in the lateral view. In the view with the occiput up portion 4 is seen to be compressed from the medial side. The third ventricle is visible only anteriorly and is pushed forward and downward. The pineal gland is calcified and pushed markedly downward and forward.

SUMMARY

We present a pneumographic study of one hundred and twenty cases of tumor of the brain in which the diagnosis was verified.

We describe a form which we have used and which we believe presents an exact and concise picture in each case from the standpoint of pneumographic analysis.

In the light of present knowledge and from the interpretation in these cases it is our opinion that a locational diagnosis of tumor of the brain can be made in more than 90 per cent of cases on the basis of study of the films alone. We base this statement on the following conclusions, derived partly from the literature, which we find substantiate our own observations, and partly from certain information which we have obtained during the study.

This analysis includes only true tumors of the brain, but it must be borne in mind that any expanding lesion, such as abscess, hemorrhage or cyst, may produce similar deformities.

CONCLUSIONS

To the conclusions given in part I of this study [1] the following may be added:

If there is a definite deformity in any part of a ventricle and it can be substantiated in films taken in a different direction or later in the series, a tumor of the brain is present in the region of the deformity, provided that a brain scar can be ruled out.

Hydrocephalus of all or any part of the ventricular system indicates a tumor of the brain (cerebral atrophy and adhesive arachnoiditis having

been ruled out). A tumor of either hemisphere nearly always causes some degree of hydrocephalus of the contralateral ventricle.

If there is a definite lateral shift of the aqueduct of Sylvius, as seen in true anteroposterior or postero-anterior films in the presence of hydrocephalus, a tumor in the posterior fossa is present on the side of the hemisphere away from the displacement; similarly, a displacement of the aqueduct of Sylvius forward or backward or of the fourth ventricle backward is significant.

If bubbles collect in a position where normally there is a clearcut outline, the diagnosis of a tumor of the brain should receive serious consideration.

EXPERIMENTS WITH QUININE AND PROSTIGMIN IN TREATMENT OF MYOTONIA AND MYASTHENIA

FOSTER KENNEDY, M.D., F.R.S.E.
AND
ALEXANDER WOLF, M.D.
NEW YORK

There is acute clinical contrast between myotonia congenita and myasthenia gravis: that of the sthenic and the asthenic; great muscles and lean ones, progressive power and progressive weakness. By Walker's [1] discovery of the effectiveness of prostigmin (the dimethylcarbamic ester of 3-oxyphenyltrimethylammonium methylsulfate) [2] in the treatment of myasthenia and the recent observation by one of us (A. W.) [3] that quinine abolishes myotonus, pharmacologic tools have become available with which to show also a chemical contrast between these two disorders.

The value of quinine in the treatment of myotonia is further established by the following brief report of four additional cases, bringing the total number in our series up to eight.

REPORT OF CASES

Case 1.—A. B., a middle-aged woman, had had myotonia atrophica for six years. Myotonus most evident in grasping movements and on percussion of the tongue, was eliminated by the administration of quinine hydrochloride, 5 grains (0.324 Gm.) twice a day by mouth.

Case 2.—H. H., a young man with myotonia congenita, exhibited the huge muscles characteristic of the disease but only a mild degree of myotonus, which was abolished by the administration of quinine hydrochloride, 10 grains (0.648 Gm.) three times a day by mouth.

Case 3.—R. S., a middle-aged man with myotonia atrophica, who had passed the stage of myotonus and showed advanced atrophy, still exhibited definite myotonia of the tongue on percussion. This disappeared with the administration of quinine hydrochloride, 5 grains three times a day by mouth.

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1. Walker, Mary: Case Showing Effect of Prostigmin on Myasthenia Gravis, Proc. Roy. Soc. Med. **28**:759-761 (April) 1935.

2. Prostigmin has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

3. Wolf, Alexander: Quinine: An Effective Form of Treatment for Myotonia, Arch. Neurol. & Psychiat. **36**:382-383 (Aug.) 1936.

CASE 4.—E. D. G., a middle-aged man, had myotonia atrophica almost identical with that in case 3 in that he exhibited lingual myotonus which responded similarly to the same dose of quinine hydrochloride.

It appears, therefore, to be a clinical fact that quinine is as specific a corrective for the symptoms of myotonia as is prostigmin for those of myasthenia gravis.

PHARMACOLOGIC ANTAGONISM

In the light of the symptom specificities of these drugs, quinine was given in several cases of myasthenia gravis, and prostigmin in cases of myotonia congenita. The ensuing increase in weakness in the cases of myasthenia and the huge increase in muscular tonus in those of myotonia were further evidence of the mutually opposed natures of these diseases. The respective effects of the drugs were never in doubt. After taking 5 grains of quinine hydrochloride by mouth two or three times a day three patients with myasthenia gravis who previously were ambulatory became bedridden and showed more rapid loss of strength in standardized tests. Two patients with myotonia congenita who had been given prostigmin demonstrated much greater difficulty in starting movement than had previously been present.

Next to prostigmin, ephedrine is the most useful drug in the treatment of myasthenia. In 1924 a case was reported in which there was response to epinephrine,[4] although our clinical observations do not confirm this work. However, we found that epinephrine and ephedrine produce extreme initial rigidity in myotonia. Ephedrine is structurally closely related to epinephrine, and, like epinephrine, it rotates light to the left; according to Sollmann,[5] the output of epinephrine is increased by the use of physostigmine. Possibly therein lies its partial effectiveness in myasthenia. It is reasonable to assume also that prostigmin exaggerates myotonus, partially at least, by releasing more epinephrine. Patients suffering from myotonia congenita occasionally tell of increased tonic difficulties under emotional excitement. This may come from release of epinephrine. The state of muscle tonus seen when persons are "paralyzed with fear" may have some relationship to this phenomenon.

Again, Sollmann stated that the twitchings produced in striped muscle by physostigmine are arrested by atropine, its pharmacologic antagonist. In this connection Weiss and one of us (F. K.) [6] reported

4. Tietz, L.: Ein Fall von Myasthenia gravis, pseudoparalytica (auf einem Adenom der Nebenniere beruhend), Klin. Wchnschr. **3**:1862-1863 (Oct. 7) 1924.

5. Sollmann, Torald: A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1936, p. 382.

6. Weiss, Soma, and Kennedy, Foster: Clinical Experiments in Myotonia Congenita (Thomsen) with Especial Reference to the Parasympathetic Nervous System, Arch. Neurol. & Psychiat. **11**:543-550 (May) 1924.

two cases of myotonia in which the symptoms improved with atropine therapy. Thus again, the use of antipodal drugs emphasizes the contrasting conditions in myasthenia and myotonia.

GLANDULAR ANTAGONISM

Peculiar endocrine phenomena are sometimes seen in these neuromuscular disorders. Lord [7] reported the case of a woman aged 23 who had periodic myotonic difficulties at the menses. She was muscularly normal as soon as the flow began.

Gardiner [8] described a boy with myotonia, aged 6 years, whose mother during pregnancy had had muscular difficulties of the myotonic type. She often fell. After delivery this trouble ceased. Her child, however, had the characteristic muscular symptoms of myotonia from birth.

Frink [9] reported a case of myotonia congenita in which the condition was improved by the giving of thymus. Wechsler [10] noted persistence of the thymus in many cases of myasthenia gravis, and in the experience of one of us (F. K.) a large, thin thymus is a characteristic observation at autopsy in cases of myasthenia gravis, the gland clothing the superior portion of the pericardium. Sir Farquhar Buzzard in 1906 directed attention to the contrast in the muscular symptoms of myasthenia and those of myotonia and observed symptomatic fluctuations during pregnancy. There is evidence that other glands, such as the adrenals, pituitary, thyroid and parathyroids, may function awry in myasthenia.

Occasionally exophthalmic goiter is associated with a myasthenic picture, yet myxedema is seen at times in cases of myotonia congenita.[11] We have clinical evidence that myasthenia gravis is made worse by the use of thyroid; on the other hand, Weiss and one of us (F. K.) [6]

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7. Lord, S. A.: Two Cases of Thomsen's Disease, and One of Transient Myotonia, Occurring in One Family, Boston M. & S. J. **142**:249-252, 1900.

8. Gardiner, C. F.: A Case of Myotonia Congenita, Arch. Pediat. **18**:925-928, 1901.

9. Frink, H. W.: Myotonia Congenita, J. Nerv. & Ment. Dis. **45**:349, 1917.

10. Wechsler, I. S.: A Text-Book of Clinical Neurology, ed. 2, Philadelphia, W. B. Saunders Company, 1931, p. 201.

11. Garcin, R.; Rouquès, L.; Laudat and Frumusan: Syndrome thomsénien et syndrome myxoedémateux cliniquement associés. Début simultané et évolution parallèle, Rev. neurol. **64**:59-72 (July) 1935. Bourguignon, G., and Garcin, R.: Syndrome thomsénien et myxœdème cliniquement associés. Début simultané, évolution parallèle; étude de la myotonie, ibid. **64**:72-82 (July) 1935. Garcin, R., and Bertrand, I.: Syndrome thomsénien et syndrome myxoedémateux cliniquement associés. Début simultané. Evolution parallèle; étude anatomique et conclusions, ibid. **64**:82-90 (July) 1935.

reported on two patients with myotonia who improved after the administration of thyroxine.

According to Bram,[12] over 95 per cent of five hundred patients with exophthalmic goiter tolerated from 30 to 90 grains (1.944 to 5.832 Gm.) of quinine sulfate every day for weeks, without cinchonism. One of our patients (J. D.) with myotonia congenita took 30 grains of quinine hydrochloride every day for two months, without cinchonism. The basal metabolic rate was normal. That specific overtoning of muscle disappears with the administration of quinine suggests that the thyroid, in primary or ancillary rôle, may be responsible for the disease.

Insulin[13] was reported as a partially successful therapeutic agent in two cases of myasthenia gravis, while one of our patients (J. D.) with myotonia congenita showed definite aggravation of symptoms after the use of insulin.

Recently anterior pituitary has been recommended in the treatment for myasthenia gravis.[14] One of the patients (H. B.) in our series is making a fair response to this therapy. A similar mild response to thyroid in cases of myotonia congenita points, through a long-recognized close association between the anterior lobe of the pituitary and the thyroid gland, to a relationship of opposition between myasthenia and myotonia.

Myotonus has been reported to be diminished by the administration of calcium, viosterol and parathyroid.[15] Recent studies[16] have indicated that the anterior lobe of the pituitary gland governs calcium metabolism, formerly believed to be controlled by the thyroid and parathyroid glands. These therapeutic relationships merely emphasize the peculiarly opposed relationship of myasthenia and myotonia. A chart illustrates more

12. Bram, I.: Relationship of Quinine Tolerance to Thyroid Secretion, Northwest Med. **30**:308-312 (July) 1931.

13. Pitfield, R. L.: Use of Insulin in Myasthenia, Tuberculosis and Other Disorders of Nutrition, M. Rec. **141**:328-331 (April 3) 1935.

14. Simon, H. E.: Myasthenia Gravis: Effect of Treatment with Anterior Pituitary Extract; Preliminary Report, J. A. M. A. **104**:2065-2066 (June 8) 1935.

15. (*a*) Menninger, W. C., and Kemp, J. E.: Myotonia Congenita: Case, M. Rec. **141**:551-553 (June 19) 1935. (*b*) Lindsley, D. B., and Curnen, E. C.: An Electromyographic Study of Myotonia, Arch. Neurol. & Psychiat. **35**:253-269 (Feb.) 1936. (*c*) Urechia, C. I.; Retezeanu and Dragomir, L.: Paramyotonie congenitale. Troubles dans les échanges du calcium sanguin. Traitement par la parathyroïde Richter, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1430-1433, (Nov. 28) 1932. (*d*) Ribadeau-Dumas, L.; Bourguignon and Lévy, M.: Atonie congénitale, hypocalcémie, amélioration remarquable par les grosses doses de stérol irradié, Bull. Soc. de pédiat. de Paris **29**:110-117 (Feb.) 1931.

16. Aub, J. C., read at the symposium on "The Central Nervous System," the Harvard University Medical School, Boston, at the Harvard Tercentenary Celebration, Sept. 15, 1936; to be published.

concisely the pharmacologic contrast between the two diseases. Some of the drugs charted are not spoken of in this paper, as their effects are still being studied.

PATHOPHYSIOLOGIC SITE

The pathophysiologic site of myotonia and myasthenia is obscure. The excessive sweating and the bluish, cold hands and feet in the cases of myotonia congenita in our series, noted also by Menninger and Kemp,[15a] seem to indicate a vasomotor unbalance. We therefore injected into the first and second thoracic sympathetic ganglia on the right side a 2 per cent solution of procaine hydrochloride in cases of these diseases. In patients with myotonia dryness and heat were noted in the right hand, but there was no effect on the preexisting myotonus. The same experiment in a case of myasthenia gravis included also

Comparison of Effects of Various Drugs in Myotonia and Myasthenia

	Myotonia	Myasthenia
Prostigmin	Markedly exaggerated	Abolished
Quinine	Abolished	Exaggerated
Physostigmine salicylate	Slightly exaggerated	Slightly improved
Ephedrine	Slightly exaggerated	Improved
Epinephrine	Markedly exaggerated	Slightly improved
Atropine	? Improved	? Exaggerated
Tincture of belladonna	? Slightly exaggerated	? Slightly improved
Glycerin	Exaggerated	? Improved
Veratrine	? Exaggerated	Improved
Thymus	Improved	? Exaggerated
Anterior pituitary	? Exaggerated	Improved
Thyroid	Improved	Exaggerated
Parathyroid	Improved	? Exaggerated
Viosterol	Improved	? Exaggerated
Calcium	Improved	? Exaggerated
Insulin	Exaggerated	Improved

injection about the stellate ganglion. The result was Horner's syndrome on the right, with the same signs in the hands, and exaggeration in fatigue. This was shown by inability to open both hands completely after alternately opening and closing them for a few minutes. The exaggerated weakness in both hands when injection was made only on one side suggests the suppression by the anesthetic of circulating "sympathetic stuff" and an extravagant response to the normally circulating "vagus stuff."

Jacoby [17] speculated regarding this matter as follows:

> Some change [may exist] in the nerves themselves, and not in the muscles, probably a change in their molecular arrangement, for microscopically the nerve terminations appear normal, and it is after all possible that later observations may discover changes either in the peripheral or central nervous system, which

17. Jacoby, G.: J. Nerv. & Ment. Dis. **14**:129, 1887; quoted in Jelliffe, S. E., and Ziegler, L.: Thomsen's Disease (Myotonia Congenita) J. A. M. A. **100**:555-560 (Feb. 25) 1933.

will take this peculiar affection out of the domain of primary muscular disorders to which it now appears to belong.

Jacoby's thesis is untenable in the light of an experiment which we devised. Spinal anesthesia was administered to a patient with myotonia congenita, as he lay on his right side; shortly afterward the right lower limb was paralyzed and insensitive to pinprick, while the left lower limb was normally sensitive and under perfect voluntary control. At this stage the myotonic reaction evident on percussion and galvanic stimulation of the gastrocnemius muscles was as profound as in the normal state and was equal on the two sides. This "toxic" muscular state remained unchanged as there gradually developed bilateral paralysis and analgesia below the sixth dorsal spinal segment. Ten grains (0.647 Gm.) of quinine dihydrochloride then given intravenously made almost undetectable the myotonic response in the gastrocnemius muscles under these anesthetic and paralytic conditions. This experiment indicates that the myotonus of myotonia congenita is a pathologic condition of the muscle or the neuromuscular junction, independent of the central nervous system, and, further, that quinine relieves myotonus primarily by direct action on the muscle or at the myoneural junction.

PHARMACOLOGIC ACTION AT THE PATHOPHYSIOLOGIC SITE

With this idea regarding the site of the morbid process in myotonia, we may attempt to formulate a concept of the character of that process in myotonia, and in myasthenia as well. Prostigmin is thought now to delay the destruction of acetylcholine by the choline esterase normally circulating in the blood. This notion, however, seems impeachable, for if heavy doses of acetylcholine are given—and it is assumed that the freely operating "vagus stuff" is the active therapeutic agent—no improvement occurs in the myasthenic symptoms. It is unlikely, though possible, that huge doses of acetylcholine can be destroyed by the choline esterase. Perhaps the action of the "vagus stuff" is disguised by its nicotine-like effects. The patients with myasthenia gravis in our series were unaffected by excessive smoking. Nicotine in large doses completely inhibits the action of acetylcholine.[18] We cannot be certain, therefore, that acetylcholine is responsible for the improvement. The same conclusion follows from the fact that mecholyl, related to acetylcholine, is the physiologic antagonist of epinephrine, which has little if any effect on myasthenic muscle.

However, some evidence on behalf of the current belief in the action of acetylcholine was brought to the problem by Stavraky.[19] He showed

18. Sollmann,[5] page 339.

19. Stavraky, G. W.: Effect of Quinine on Parasympathetic and Sympathetic Innervation of the Salivary Glands, J. Pharmacol. & Exper. Therap. **47**:321-338 (March) 1933.

that quinine poisons the parasympathetic nerve endings of the chorda tympani. Stimulation of this nerve and of the "vagus stuff" does not then have the same effect on the salivary glands as under normal conditions. In other words, quinine neutralizes the secretory effect of choline and acetylcholine on the submaxillary gland. On the other hand, physostigmine restores the action of a parasympathetic nerve which has been poisoned by quinine. Stavraky's pharmacologic study seems precisely applicable to our problem. Quinine—a depressant for the terminations of the vagus nerve—weakens myasthenic muscles by inhibiting the "vagus stuff."

Sollmann [5] stated that twitchings produced by physostigmine persist after section of a motor nerve, such as the sciatic. These twitchings are suppressed by curare, an antagonist of physostigmine.[20] The antagonism between physostigmine and curare must mean, therefore, that physostigmine acts at the myoneural junction. It is probable from Stavraky's observations that quinine acts at the same point.

From this pharmacologic evidence it appears that prostigmin is effective in myasthenia through its catalytic influence on acetylcholine, while quinine is effective in myotonia through its inhibition of acetylcholine, both acting at the myoneural junction. No doubt, however, there are other factors at work, perhaps endocrine, of which there is as yet little or no knowledge.

CONCLUSIONS

Quinine is as effective in myotonia as is prostigmin in myasthenia.

The clinical contrast between myotonia and myasthenia is confirmed by the exaggeration of myotonus by prostigmin and of myasthenia by quinine. The actions of other drugs are supporting evidence for this belief.

Myasthenia and myotonia are primary disorders of muscle or the myoneural junction.

Prostigmin facilitates the action of the "vagus stuff" in myasthenia, and quinine inhibits this action in myotonia—at the myoneural junction.

Endocrine disorders little understood are at work in these maladies.

We hope that the established action of two drugs of opposite incidence in two disorders equally opposed may lead to increased knowledge of the physiologic nature of muscle contraction and that our work, in addition to that of Walker on prostigmin in the treatment for myasthenia, may aid biochemists to discover more of the nature of the nerve impulse.

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20. Walker, M. B.: Treatment of Myasthenia Gravis with Physostigmine, Lancet **1**:1200-1201 (June 2) 1934.

PATHOGENESIS OF THE CORTICAL ATROPHY OBSERVED IN DEMENTIA PARALYTICA

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It is universally recognized that the cortical atrophy observed in dementia paralytica may be entirely independent of the inflammatory phenomena. Jahnel,[1] in a recent authoritative review of the subject, stated: "The parenchymal degeneration corresponds neither in its intensity nor in its extent with the infiltrative processes." The mechanism of production of the inflammatory changes is obvious, but the sequence of events leading to the degeneration of ganglion cells has been the subject of much discussion. It has been supposed, for example, that the nerve cells are actually invaded and destroyed by the spirochetes. This appears unlikely, since, according to Jahnel,[1] spirochetes have never been satisfactorily demonstrated within ganglion cells. Also, spirochetes are usually rare or absent from areas showing the greatest degree of cortical atrophy,[2] and they have never been observed free in the white matter, even in cases in which there were extensive lesions of the white matter.[2] Another theory is that the cells are damaged by soaking with toxic material [3]—a hypothesis difficult either to prove or to disprove. The suggestion that the parenchymal changes are due to changes in the blood vessels has been made by various pathologists, especially during the pioneer period of the study of the disease. A long

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From the Neurological Unit, the Boston City Hospital, and the Department of Neurology, Harvard University Medical School.

1. Jahnel, F.: Pathologische Anatomie der progressiven Paralyse, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11.

2. Merritt, H. H., and Springlova, M.: Lissauer's Dementia Paralytica: A Clinical and Pathologic Study, Arch. Neurol. & Psychiat. **27**:987 (May) 1932.

3. Gennerich, W.: Die Syphilis des Centralnervensystems, Berlin, Julius Springer, 1922.

list of these investigators is given in Alzheimer's monograph.[4] At present, when disease of the blood vessels is mentioned, it is usually taken in the sense of inflammation, and a distinction between the effects of endarteritis and those of periarteritis is not clearly drawn. It is our purpose in the present study to investigate the possible rôle of obstruction of blood vessels in the production of the cortical atrophy characteristic of dementia paralytica.

The study has been divided into three parts: first, observations on the condition of the endothelium in cases of dementia paralytica; second, a comparison of the capillary architecture of sections from the cortex of patients suffering from dementia paralytica with that of homologous areas from normal brains by means of specific erythrocyte stains, and, third, a comparison of the cortical atrophy produced in animals by occlusion of venules and capillaries with that occurring in cases of dementia paralytica in man.

ENDOTHELIUM OF SMALL VESSELS OF THE CORTEX

Practically all authors who have described the pathologic characteristics of dementia paralytica have referred to changes in the endothelium. Alzheimer,[5] for example, stated:

> In all cases of dementia paralytica proliferative changes in endothelial cells are observed, sometimes less marked, sometimes extremely evident. While the endothelial cells of normal vessels stain only feebly with aniline dyes—their flat nuclei containing a few small chromatin granules and the cell bodies remaining unstained except for a few globules of fat or pigment—one sees in cases of dementia paralytica numerous endothelial cells with strikingly large, round or oval nuclei, rich in chromatin, and clearly evident cell bodies of reticulated or lace-work structure. Rarely, but fairly often in suitable preparations, mitotic figures may be observed in endothelial cells.

There is no difficulty in substantiating these observations. The changes described were noted in all the nine cases which we reviewed. Hypertrophied endothelial cells, apparently obstructing the lumen of the vessel, are reproduced in figure 1. Alzheimer's[4] illustrations (plates II and III) show many similar examples.

The question of the cause of the hypertrophy of endothelial cells may be raised. In many instances spirochetes (fig. 2) and iron-containing pigment may be seen within the cells. It is possible that the hypertrophy is in part a phagocytic phenomenon.

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4. Alzheimer, Alois: Histologische Studien zur Differentialdiagnose der progressiven Paralyse, in Nissl, F.: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1904, vol. 1, p. 18.

5. Alzheimer,[4] page 40.

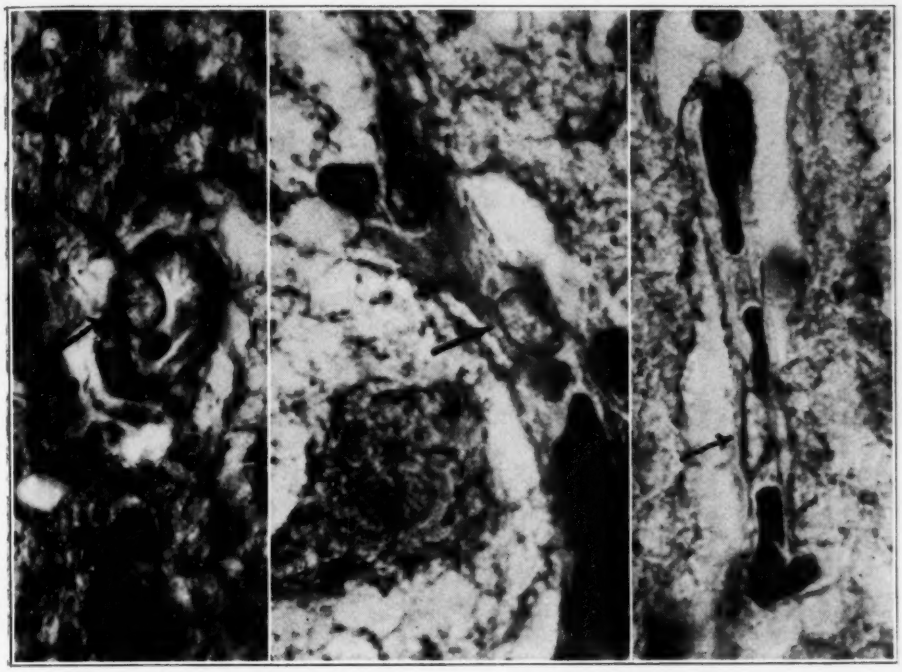

Fig. 1.—Sections taken in two cases of dementia paralytica showing hypertrophied endothelial cells (indicated by arrows) obstructing the column of blood in capillaries. Masson stain; oil immersion.

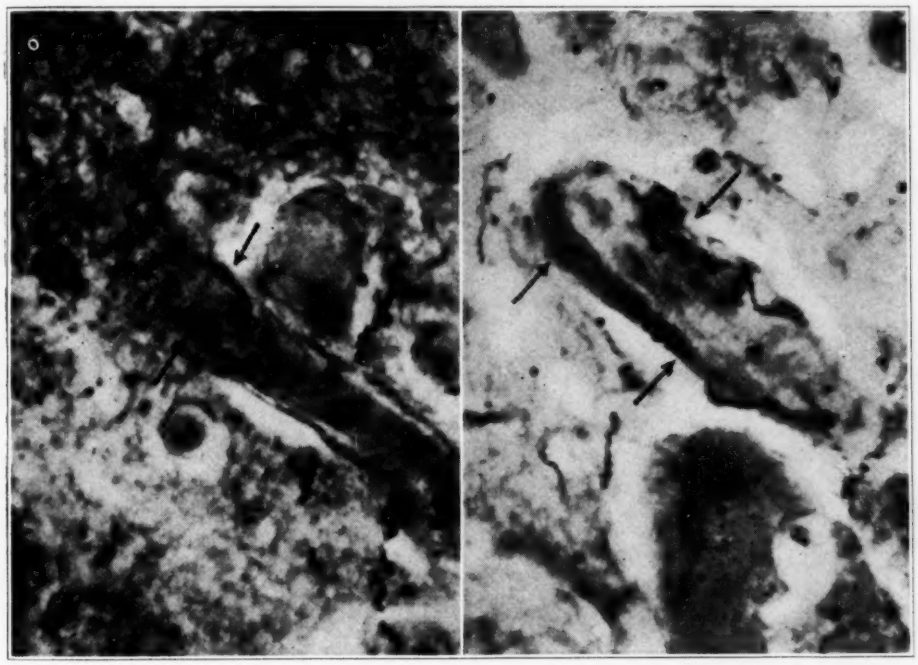

Fig. 2.—Swollen endothelial cells containing spirochetes (indicated by arrows). Jahnel stain; oil immersion.

ABNORMALITIES IN THE CAPILLARY ARCHITECTURE

The statement is often made that there is an increase in the number of capillaries in the cortex in dementia paralytica. In sections stained with aniline dyes from brains affected with this disease one often gets the impression that more vessels are visible than in similar areas of normal brains. The silver impregnation methods for connective tissue also show an abnormally dense network in the atrophic cortex. Jahnel [6] appeared to be justified in stating:

> On study of sections from areas in the cortex which are markedly affected by dementia paralytica, one is impressed with the appearance of richness of vessels. The question immediately presents itself as to whether this increase is real or only apparent. . . An actual count of the number of vessels in a given section is of no value in deciding this question. . . The opinion that the increase in the number of vessels in dementia paralytica is only apparent and relative has, indeed, found many advocates.

Lack of knowledge concerning the normal capillary architecture of the brain has recently been remedied by Pfeifer's [7] remarkable studies on injection of the capillaries of the brain. More recently, methods have become available which permit similar studies to be extended to pathologic material.[8] The stain which has given us the most striking results is Pickworth's modification [9] of Lepehne's [10] stain. It has been possible to apply this in only two cases of dementia paralytica, since fresh material is essential. Stains of the acid fuchsin type, however, have been used in seven additional cases, with consistent results. Care was taken to compare each specimen with a section of the same thickness from a homologous area in a normal brain, stained in the same manner. In all instances, a continuity of the vascular network was taken as a criterion of adequate filling with blood.

In satisfactorily filled areas from all nine brains, suitable stains demonstrated clearly that the cortical atrophy was invariably accompanied by a decrease in the number of small vessels containing blood. This is illustrated in figure 3, from specimens stained by Lepehne's method. The only exceptions to this rule were in the rare instances in

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6. Jahnel,[1] page 435.

7. Pfeifer, R. A.: Grundlegende Untersuchungen für die Angioarchitektonik des menschlichen Gehirns, Berlin, Julius Springer, 1930.

8. Putnam, T. J.; Alexander, L., and Campbell, A. C. P.: The Vascular Pattern of Various Lesions of the Human Central Nervous System: Studies with the Lepehne-Pickworth Stain, Arch. Neurol. & Psychiat., to be published.

9. Pickworth, F. A.: A New Method of Study of the Brain Capillaries and Its Application to the Regional Localization of Mental Disorder, J. Anat. **69**:62, 1934.

10. Lepehne, G.: Zerfall der roten Blutkörperchen beim Icterus infectiosus, Beitr. z. path. Anat. u. z. allg. Path. **65**:183, 1919.

which a small area of complete softening had occurred. This was always marked by localized vascular proliferation—a sort of granulation tissue.

It appears that there is not only a decrease in the number of capillaries in the atrophic cortex but a qualitative alteration in the vas-

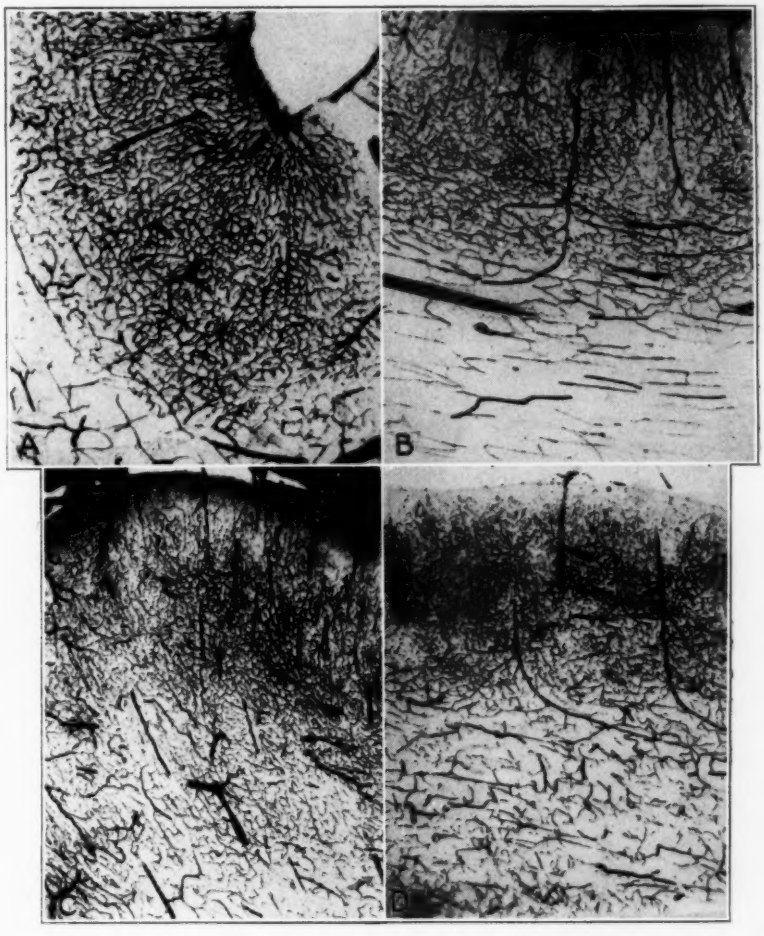

Fig. 3.—Vascular architecture of the normal cortex of the frontal lobe (*A*) and (*C*), as compared with that of similar areas (*B* and *D*) in cases of dementia paralytica. The lack of filling of capillaries in the subpial zone shown in *D* is a common artefact. Lepehne's stain; sections 100 microns thick; lens enlargement.

cular pattern. Large arteries stand out with unusual prominence; there is relative accentuation of the channels running parallel to the meninges, and long anastomotic channels of greater than capillary size seem more than ordinarily common. Tortuous, "corkscrew" veins and venules are

often striking. In view of the small number of cases studied, however, too much emphasis should not be placed on these observations.

The new data thus obtained relate only to capillaries containing blood. It is, of course, likely that many of the obstructed vessels persist and that a certain amount of endothelial proliferation occurs.

PRODUCTION OF CORTICAL ATROPHY BY EXPERIMENTAL OBSTRUCTION OF VENULES OF THE CORTEX

An attempt was made to produce lesions in the brains of dogs by obstructing the smaller cortical vessels. The technic used has previously been described by one of us (T. J. P.).[11]

The superior longitudinal sinus was exposed, and two sutures were applied to it about 1 cm. apart. A needle was inserted into the occluded portion of the sinus, and viscous substances were injected in order to produce a retrograde obstruction of the smaller veins (and possibly the capillaries) draining into the sinus.

This experiment was performed on six dogs. A viscous solution of shellac was used in dogs 1, 2, 4 and 6, a solution of hemoglobin in dog 3 and air in dog 5.

Dog 1.—After injection of 0.3 cc. of shellac there developed convulsive seizures and weakness of the legs, and the animal died eighteen days after the operation.

Dog 2.—Five days after injection of 0.3 cc. of shellac the animal had several convulsive seizures. He appeared fairly well until eighteen days after the operation, when he died, presumably after another convulsive seizure.

Dog 3.—After injection of 0.4 cc. of a solution of hemoglobin the animal was apparently unaffected. He was killed two weeks after the operation. The brain was normal.

Dog 4.—About thirty-six hours after injection of 0.5 cc. of shellac the animal was found dead. Necropsy showed that a portion of the shellac had been injected directly into the cortex.

Dog 5.—After injection with 1 cc. of air the animal was lethargic, tended to lie in the cage with his head buried in his legs and showed some difficulty in walking. He was killed after two weeks.

Dog 6.—Four days after injection with 0.4 cc. of shellac the animal showed great difficulty in walking and began to have frequent convulsive movements of the trunk and extremities; there was apparently complete paralysis thirteen days after the operation. The convulsive movements continued intermittently until death, eighteen days after the operation.

Histologic Changes.—Lesions were observed in the cortex in all the animals except dog 3. The brain from dog 4 was discarded because some of the shellac had been injected directly into the brain substance. In dogs 1, 2, 5 and 6 the lesions were numerous and of a similar nature. In all these animals there was a mild degree of meningeal infiltration with round cells. The blood vessels of the cortex showed a mild degree of perivascular infiltration with microglia cells and occasional lymphocytes (fig. 4). There was proliferation of the endothelial cells of the smaller vessels, producing a mild degree of endarteritis (fig. 5). Pigment was observed in the walls of some of the vessels. Iron pigment could be demon-

11. Putnam, T. J.: Studies in Multiple Sclerosis: IV. "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, Arch. Neurol. & Psychiat. **33**:929 (May) 1935.

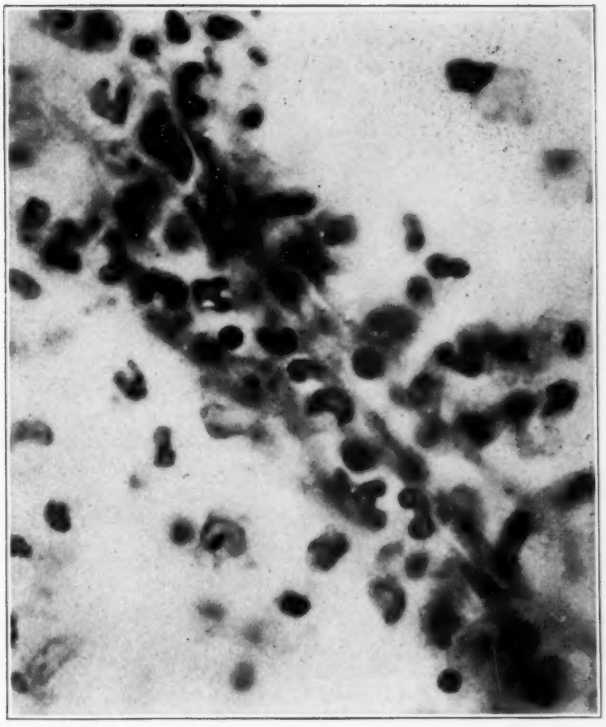

Fig. 4.—Area of cortical atrophy from dog 1, showing infiltration with microglia cells and perhaps a few lymphocytes. Cresyl violet stain; lens enlargement.

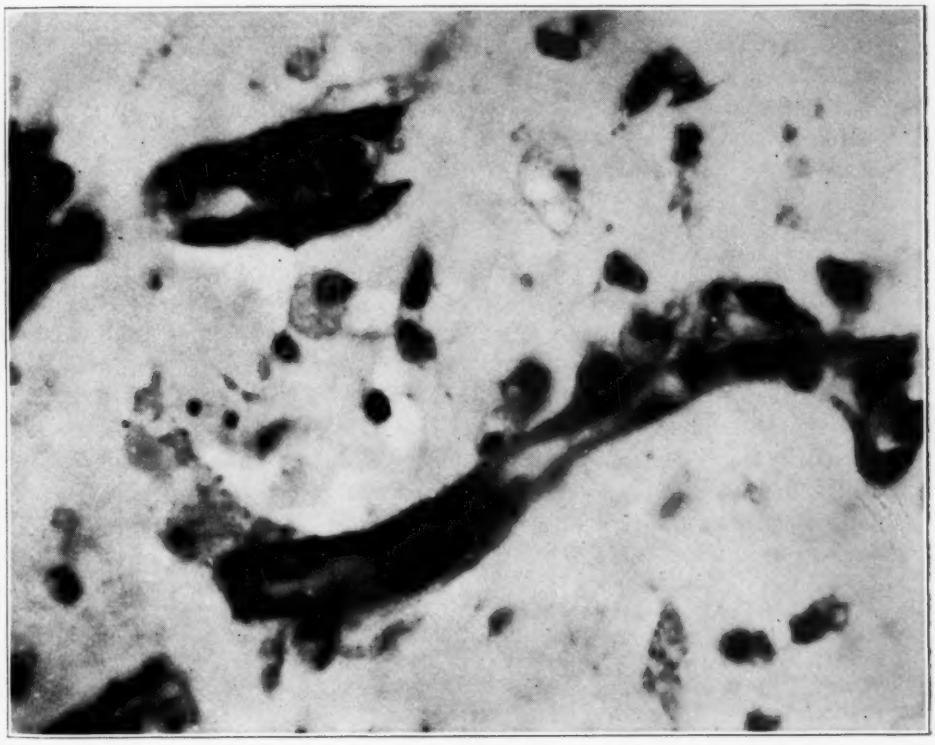

Fig. 5.—Endarteritis of a venule of the cortex in dog 1. Cresyl violet stain; high power enlargement.

strated by the Turnbull blue method (fig. 6) and by micro-incineration. The Cajal stains showed proliferation of the macroglia, and proliferation of the microglia was seen in sections stained with hematoxylin and eosin and with Nissl's method. Many rod cells were present (fig. 7). There was diffuse degeneration of the parenchyma of the cortex, which was so intense in places that practically all the nerve cells had disappeared (fig. 8). In some sections the nerve cells showed severe changes, with loss of the nucleus and liquefaction of the cell body (fig. 9); in other sections the nerve cells showed typical ischemic changes, i. e., loss of the pyramidal shape, elongation of the cell body and hyperchromatosis of the nucleus and cytoplasm (fig. 9). Diffuse and circumscribed loss of myelin was observed in the white matter of the brain in all these animals, similar to that previously reported by one of us (T. J. P.[11]). A loss of the cells in the cornu ammonis (typical cornual sclerosis) was observed in dog 6.

In summary, the lesions produced in these dogs consisted of: (1) meningeal and perivascular infiltration, with proliferation of the endothelial cells and presence of iron pigment; (2) proliferation of macroglia and microglia, with numerous rod cells, and (3) degenerative changes in the parenchyma (gray and white matter). In addition to these individual changes, which are observed in all typical cases of dementia paralytica, the general picture in the sections from the animals was strikingly similar to that seen in brains affected with dementia paralytica.

Considering the rapidity of the pathologic process in the animals in our series, it is remarkable that the parenchymatous changes were so similar to those of dementia paralytica. In dementia paralytica the process is slow, with progressive involvement of the smaller cerebral vessels, whereas in the experiments on animals all the involved vessels were injured simultaneously. It is not surprising, therefore, that the parenchymatous changes were more uniform in the animals than in the usual cases of dementia paralytica. In some of the sections from the animals, however, well preserved ganglion cells were intermingled in places with the degenerated cells.

Another point worthy of note is the presence of iron pigment in the walls of the vessels of the animals in our series. The amount of this pigment was not as great as that usually observed in sections in cases of dementia paralytica, but this may possibly be due to the short duration of the disease process in the animals. The distribution of the iron pigment in these animals is significant in regard to the hypothesis of its specificity for dementia paralytica and possibly indicates that such a distribution is significant only of a particular pathologic process and not of a disease entity. This view is supported by the observation of Wertham[12] of the typical dementia paralytica iron in the brains of birds suffering from encephalitis.

12. Wertham, F.: Zur Frage des Eisenbefundes bei der Dementia paralytica auf Grund vergleichend-histopathologischer Untersuchungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:62, 1931.

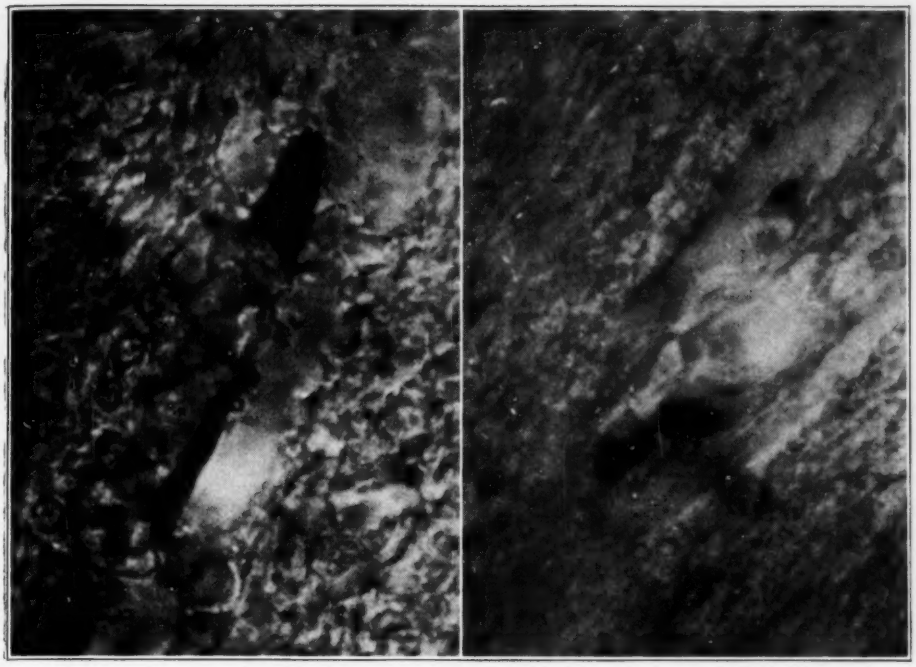

Fig. 6.—Iron pigment in the endothelial cells of the cortex in dog 1. Turnbull blue stain; high power enlargement.

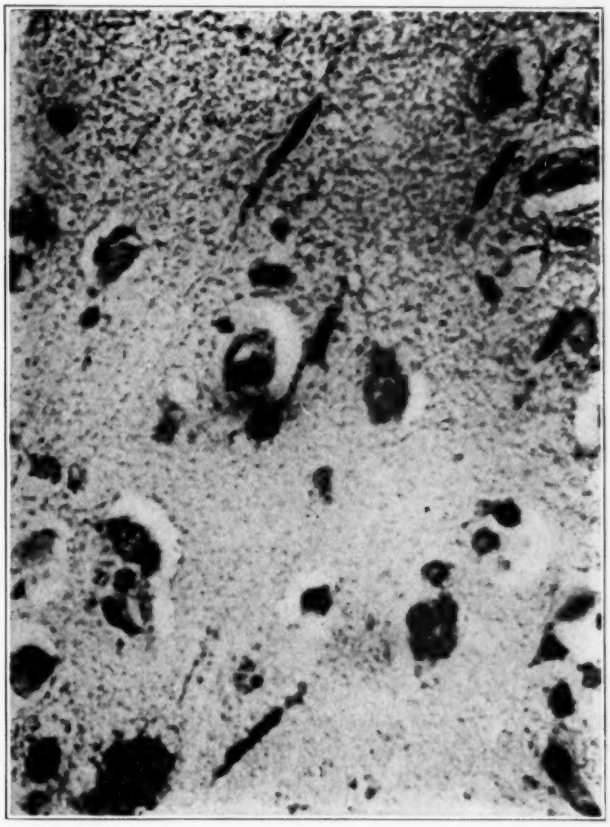

Fig. 7.—Group of rod cells in the atrophic cortex of dog 1. Cresyl violet stain; high power enlargement.

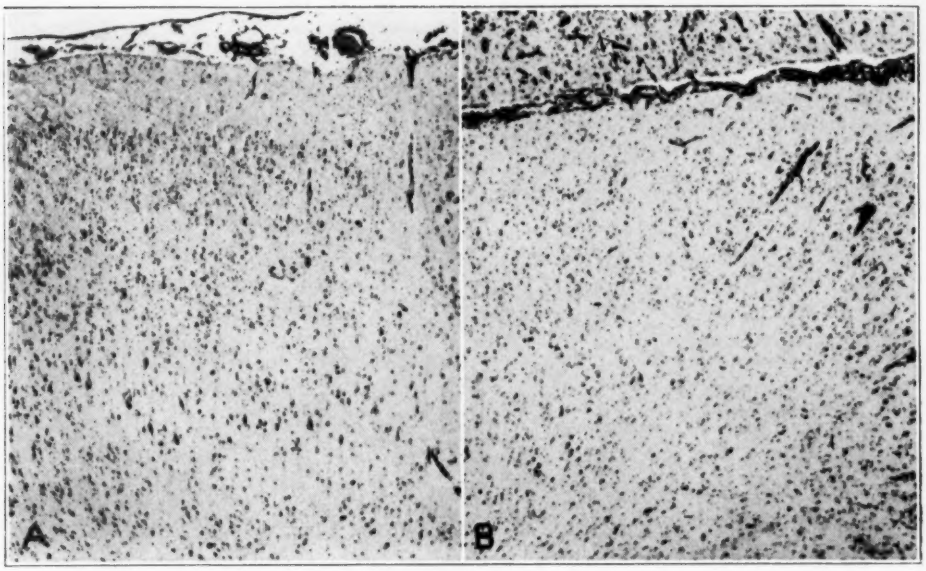

Fig. 8.—Atrophic area in the cortex in a case of dementia paralytica (*A*) compared with that in the cortex of a dog after experimental venular occlusion (*B*). Cresyl violet stain; lens enlargement.

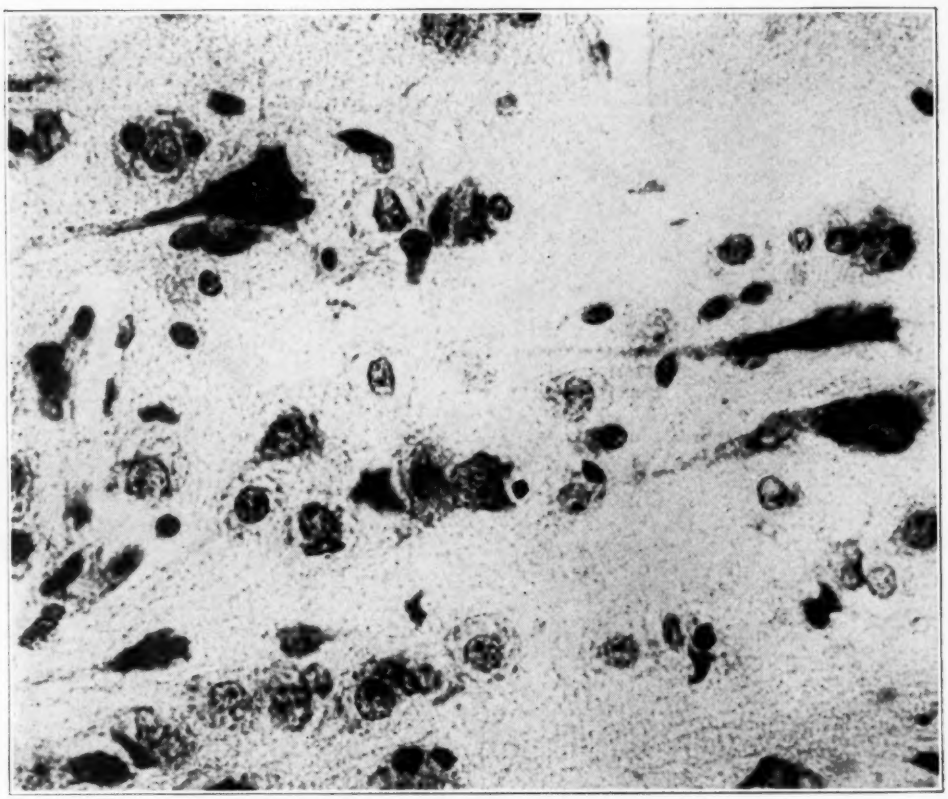

Fig. 9.—Nerve cells in various stages of degeneration from the cortex of dog 6. Cresyl violet stain; high power enlargement.

COMMENT

Endothelial hypertrophy and vascular obstruction have long been recognized as characteristic and fundamental manifestations of syphilitic infection. It has been supposed that the peculiar structure of gummas is the result of gradual local anoxemia, combined with low grade inflammation. The regressive changes in the anterior horn in the syphilitic type of progressive muscular atrophy have already been ascribed to the occlusion of capillaries by endarteritis.[13] There should be no occasion for surprise if a similar process in the cortex leads to similar results. Senile cortical atrophy, which is probably due to a decrease in blood supply, may closely imitate the atrophy of dementia paralytica. Arguments for the anoxemic origin of the cortical degeneration may thus be brought from several sides.

It is conceivable that such a point of view may have importance in planning therapeutic methods. The effectiveness of treatment with hyperthermia, for example, may be due to the prolonged dilatation of cerebral vessels. Perhaps even more effective methods of accelerating blood flow in the cortex may be devised.

CONCLUSIONS

Atrophy of the cortex, largely independent of the amount of signs of local inflammation, is the outstanding characteristic of the pathologic changes in dementia paralytica, which distinguishes it from other syphilitic diseases of the brain.

Many of the cortical capillaries in brains affected with this disease are obstructed by swollen endothelial cells, as has been pointed out by practically all observers. The hypertrophied endothelium often contains phagocytosed spirochetes and blood pigment.

By suitable staining methods it can be demonstrated in sections in cases of dementia paralytica that the number of capillaries containing blood is greatly diminished, as compared with that in homologous areas in normal brains.

Experimental obstruction of venules and capillaries of the cortex in dogs produces local degeneration characterized by regressive changes in nerve cells and, finally, by their complete disappearance over large areas; deposit of iron pigment; formation of rod cells, gliosis, and perivascular accumulation of phagocytes and occasional lymphocytes. The resulting picture as a whole and in detail resembles that seen in cases of dementia paralytica.

It is suggested, therefore, that the degenerative changes in the cortex in dementia paralytica may be regarded as secondary to anoxemia produced by endarteritis of small vessels.

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13. Martin, J. P.: Amyotrophic Meningo-Myelitis (Spinal Progressive Muscular Atrophy of Syphilitic Origin), Brain **48**:153, 1925.

DISCUSSION

DR. HARRY C. SOLOMON, Boston: The explanation for the loss of the nerve cells in dementia paralytica presented by the authors is novel, intriguing and challenging. It also discloses considerable ingenuity, particularly on the experimental side. Whether the conclusions are sound and can stand is a matter, however, that one may question.

That there is thickening of the endothelium is obvious. That there is a loss of permeability of the capillaries I am not so sure. It is characteristic of the vascular bed that it can hold much more or much less blood under varying circumstances. In an ordinary piece of brain tissue, that is, from a patient who does not have dementia paralytica, there is little evidence of an expanded vascular bed, but rather an absence as far as one can see, of much vascular area. Yet it is known that if this space is opened under other conditions it may contain a great deal more blood.

I wonder whether vessels which present swollen endothelium are not still quite permeable and whether they do not supply all the blood that is required in the denuded area. The very fact that the area is denuded of the primary cells that require blood would necessarily result, I think, in a need for a smaller blood supply. De Sylvia has shown some illustrative pictures, it being his contention that in the regions where the nerve cells have disappeared one never finds spirochetes but that they apparently wander into new territory, where there are other cells to be attacked.

Another point that seems to me of considerable interest is in regard to the experimental cases. There is destruction of nerve cells, but the picture is not identical with, although it is similar to, that seen in dementia paralytica. As far as I was able to see the slides and photographs, no normal cells are present in regions in close proximity to sick or dying cells, as is so common in the picture of dementia paralytica.

Finally, I am struck with the fact that in dementia paralytica, in contrast to arteriosclerotic conditions, there is no relationship between loss of cells and vascular supply; that is, definite perivascular lesions are not seen. There are relatively few softenings, and they occur only in exceptional cases of dementia paralytica. Nor does one find a picture similar to that of arteriosclerosis of the larger blood vessels, even when there are arteriosclerotic changes in the fine blood vessels. I think, therefore, that there is a difference between the picture of dementia paralytica and these experimentally produced lesions; so one may well question whether the authors are right. This is a stimulating and challenging paper, attempting to elucidate a process which I believe has heretofore been unsatisfactorily explained, if it has been explained at all.

DR. FREDERIC WERTHAM, New York: This is an important contribution to the subject of the pathologic anatomy of the brain. If I understand the course of events correctly, it represents the confluence of two streams of investigative interest. The members probably are familiar with the report of Dr. Merritt on the focal lesions in dementia paralytica, in which he made some suggestions about the importance of the blood vessels in the distribution of Lissauer's dementia paralytica. The other stream, as I see it, is represented by Dr. Putnam's interest in the results of what happens in the blood vessels that do not do what they should, or what he thinks they should.

Rarely are experimental studies on the histopathologic characteristics of mental diseases undertaken, and even more rarely are they undertaken without any attempt at correlation with the clinical symptoms. I think one of the merits of this paper is that it does not tell what the clinical correlations are, especially since it is not known what correlation there is between the lesions and the mental symptoms in dementia paralytica.

Observations on diseases of animals similar to dementia paralytica have often been made. But in experimental conditions modern methods have not been applied except in my studies on the subject and in this one. For the most part these observations were on spontaneous diseases. Nissl, about forty years ago, saw in rabbits an encephalitis the picture of which looked much like what one then had to consider as the lesions of dementia paralytica, and Dr. Meyer's famous hog, a report on which he never published but of which he tells his pupils, showed lesions similar to those in dementia paralytica. As far as the infiltrations were concerned, the lesions were indistinguishable.

The present view of dementia paralytica is somewhat different. I think neurologists have learned that one of the most important histologic signs is "iron." Many details in this paper might be discussed, but I wish to say a few words about that. It is interesting that in this study there were other lesions besides certain observations of "iron." If one mentions the word "iron" in connection with histologic structure, I think one should put it in quotation marks, especially after the paper by Dr. Alexander in which he said that in his interesting dark field studies he did not observe "iron" with the incineration method where one would expect to see it. This points to the fact that there are different kinds of "iron." It is known, for example, that in every normal brain certain nuclei can be distinguished from the "iron" in the microscopic section. The "iron" observed in dementia paralytica, which, as Dr. Merritt pointed out, I saw for the first time in animals, i. e., in birds with spontaneous disease, is different. I want to point out only one difficulty, which probably Dr. Merritt can settle. The "iron" in dementia paralytica has certain definite qualities by which one may recognize it among the different kinds of "iron" known histologically. It occurs in the intra-adventitial spaces and also in hypertrophied Hortega cells in the central nervous system—so-called rod cells. The interesting point is that it has another quality, one which I consider the most important, and that is its diffuse distribution. In dementia paralytica, whenever one finds other lesions, spirochetes, infiltrations and rod cells one also observes this "iron." Under experimental conditions, since only a certain part of the blood supply can be eliminated, a focal lesion is produced. For that reason alone one must conclude that the "iron" present is totally different from the "iron" in a case of dementia paralytica and from that observed by me in birds.

"Iron" always occurs in vascular lesions and in the neighborhood of the lesions. The question arises: Can one ever produce it experimentally in diffuse distribution, and can one compare the "iron" produced experimentally with that which appears in dementia paralytica? I shall be interested in Dr. Putnam's remarks, for if "iron" can be produced experimentally, the neuropathologist has progressed beyond studying disease in a hog or a rabbit and has come a little nearer to producing experimentally lesions which look like those of dementia paralytica.

This paper presents in an interesting way a problem that was discussed after Dr. Ferraro's paper. It shows the utter confusion about specificity and the claim that if the source of a lesion is known the disease is understood. This claim is not valid, for, after all, dementia paralytica is caused by spirochetes and the spirochetes have been seen; but despite the fact that the source is known and the

lesions have been seen, it is not known how they come about. It would be better if, instead of "lesion," Dr. Meyer's term "postmortem symptomatology" were used, as a reminder that the symptoms which occur before death, must all be reviewed in the light of the postmortem appearance of the lesions. The question still remains: What is the actual process that goes on? I think that under experimental conditions by the elimination of blood supply one comes much nearer to a process, which is what the neuropathologist is interested in.

This paper has a connection with the paper on oligodendroglia; i. e., an attempt has been made to connect schizophrenia and other conditions with a histologic lesion, the swelling of the oliogodendroglia cells. I agree with Dr. Meyer when he said that one has to remember that in this work only one histologic element was studied. But I believe that one should remember that not just one element but something completely static is placed under the microscope. In my opinion it is hazardous to correlate a chronic clinical process with a static observation. Studies like this one may throw light not only on dementia paralytica but actually on the theoretical conception of histopathologic processes.

Dr. Leon H. Cornwall, New York: There can be no question that one gets the impression in the high power examination of a field that there is an increase in the number of blood vessels as compared with that in normal brain tissue. I do not believe one can doubt that anoxemia is an adequate cause of some of the cellular alterations. It is known to be a cause of degeneration of ganglion cells and for atrophic changes in the brain and elsewhere in the central nervous system. From the study of individual vessels it is certain that endothelial hyperplasia and extensive changes in the intima are constantly observed in cases of dementia paralytica. Therefore, it seems to me that the conclusions Dr. Putnam has drawn that the atrophy of the brain and cellular changes are due in part to lesions in the blood vessels and consequent anoxemia are valid. To be sure, as Dr. Solomon suggested, it may be difficult to prove that the actual volume of blood is reduced, but it seems to me that the morphologic evidence is all in favor of this theory. Dr. Putnam has made a valuable contribution to the program of this association and to the pathology of dementia paralytica.

Dr. Tracy J. Putnam, Boston: Dr. Merritt, Dr. Campbell and I feel not that we have reached a conclusion about dementia paralytica but that we have something to think about in the chain of events between the invasion of the nervous system with spirochetes and the dropping out of the nerve cells. It seems to us also that, as Dr. Wertham has so well put it, it would be better in difficult pathologic situations to try to divide the problems into as short and as small units as possible and to study each one separately. We put these data forward only as suggestive evidence.

In regard to Dr. Wertham's question about the distribution of iron, we certainly cannot claim that we have produced a distribution of iron in these animals entirely parallel to that seen in human beings with dementia paralytica. There is some iron in the tissues, but I think it is conceivable that the process in human beings with dementia paralytica, since it is not produced immediately by a rather crude surgical manipulation but advances from capillary to capillary, possibly over a series of years, may produce quite a different type of saturation of the tissues with iron.

In connection with other studies, I have been struck by what Dr. Wertham also mentioned: the different types of iron that are observed in tissues and the various changes in iron pigment. It is possible that the peculiar situations which

exist in dementia paralytica make the production of peculiar forms of iron unusually common. I think that as far as demonstrating iron in general is concerned, Dr. Alexander's micro-incineration studies have provided the most valuable method, for they demonstrate iron in no matter what form it is. It exists in a great many more forms than are demonstrable by ordinary chemical tests, and I feel considerable confidence in his observations after following them through a number of different conditions. Dr. Wertham spoke of the interest of Dr. Merritt and myself, and he should not forget that of Dr. Campbell, who brought neurologists the technic of the Pickworth stain and taught them a great deal about differentiating types of vascular architectural changes in various diseases, without which help our conclusions would be even less definite than they are, for the changes in vascular pattern are quite striking. I do not know that we have studied enough cases to be sure how constant our conclusions are, but in the few cases we have observed the facts seem to be convincing.

To answer Dr. Solomon's question: There are types of destruction in nerve tissue in which the circulation, that is, the number of functioning capillaries, does not seem to be decreased. My co-workers and I have seen softenings of this type, in which the parenchyma is wiped out but the capillary network is increased rather than decreased.

In regard to spirochetes in nerve cells, I have had a limited experience, but in the preparations I have seen I have not observed them. I think it is difficult to be sure whether or not a spirochete lies in a cell. We had difficulty making up our minds in connection with endothelial cells. There, at least, one is on slightly firmer ground, for one can find sections cut transversely so that the cell forms a narrow line and yet the spirochete may lie within it.

As to the adequacy of loss of circulation to cause the changes seen in dementia paralytica, I wish to refer to a fact concerning normal anatomic structure which has become definite only since Pfeifer's studies and which we have substantiated in our own laboratory, namely, the relationship between capillaries and large nerve cells. It was first pointed out to me by Dr. Frank Fremont-Smith that every large nerve cell seems to have a capillary all its own, which does not supply anything else. The smaller cells may be grouped along a capillary and even at some distance from the capillaries. The large cells almost without exception lie directly on a capillary. It is hard to believe that this does not have a functional correlation and that the closure of the capillary would not lead to the death of the cell.

As to the spotty nature of the degeneration in dementia paralytica, I should question first whether this is general. In the preparations which we have complete degeneration of nerve cells does occur in some parts of the specimen, and I may say that in the experimental dogs spotty and incomplete destruction of nerve cells occurred in some regions but was not nearly so picturesque as complete destruction and for this reason was not used for reproduction. However, it is possible to find fields showing complete destruction, moderate destruction or perivascular infiltration, so that it is difficult to tell whether one is looking at a canine or a human specimen.

I think one must draw a distinction between obstruction of vessels of this type which is largely or wholly limited to capillaries, and that which follows the occlusion of larger arterial trunks. For some reason, the conceptions of vascular disease are practically all founded on the occlusion of arterial trunks. It is as though one neglected to realize that there were any capillaries in the brain and that the blood in those capillaries had to be carried out by veins. My own observations have led me to the strong belief that different types of vascular occlusion produce

quite different and often characteristic parenchymatous disturbances. As a matter of fact, I think arteriosclerotic brains are occasionally seen in which the changes in the nerve cells are difficult to distinguish from those of dementia paralytica.

I find my interest aroused by the relation of dementia paralytica to multiple sclerosis. The similarity between the two conditions has often been pointed out and is certainly striking in selected instances. It is on this account that multiple sclerosis has often been considered an infectious spirochetal disease. It is of interest to find how far one can go by turning the tables and seeing how much of the pathologic change of dementia paralytica can be explained on a mere mechanical basis.

SYNDROME OF THE ANTERIOR SPINAL ARTERY OF THE MEDULLA OBLONGATA

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In previous communications on the syndromes of the cerebellar arteries [1] it was shown that, in contrast to cerebral vascular insults, occlusion of the cerebellar vessels is rare. Closure of the upper part of the anterior spinal artery supplying the medulla oblongata is even less common. Involvement of this vessel was found in only two instances in a series of about four hundred cases of cerebrovascular disease which came to autopsy.

In contrast to the frequent anomalies of the posterior inferior cerebellar arteries, anomalies of the upper portion of the anterior spinal and of the vertebral arteries are less commonly observed. The variability of the symptoms occurring with occlusion of the vertebral artery depends on whether the posterior inferior cerebellar artery arises from the basilar or from the vertebral artery. When this cerebellar vessel has origin from the vertebral artery, it is difficult to state whether the symptoms are due to occlusion of the posterior inferior cerebellar or to occlusion of the vertebral artery. This is especially true if the anterior spinal artery of the medulla oblongata is not involved. The associated implication of the latter results in the additional destruction of one or both pyramids, the medial lemniscus and occasionally the fibers of the hypoglossal nerve, resulting in the so-called syndrome of the anterior spinal artery of the medulla oblongata. This syndrome consists of contralateral pyramidal tract signs of the trunk and upper and lower extremities, contralateral loss of discriminative sensibility in the upper and lower extremities and body, and occasionally in ipsilateral paralysis and atrophy of the tongue. In the presence of only one anterior spinal artery, both pyramids and medial lemnisci may be involved. At times the pyramids may receive blood supply directly from the vertebral artery.

From the Neurological Division and the Neuropathological Laboratory of the Montefiore Hospital.

Read by title at the Sixty-Second Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 2, 1936.

1. (*a*) Davison, C.; Goodhart, S. P., and Savitsky, N.: Syndrome of the Superior Cerebellar Artery and Its Branches, Arch. Neurol. & Psychiat. **33**:1143 (June) 1935. (*b*) Goodhart, S. P., and Davison, C.: Syndrome of the Posterior Inferior and Anterior Inferior Cerebellar Arteries and Their Branches, ibid. **35**:501 (March) 1936.

A careful search of the literature on thrombosis of the anterior spinal artery of the medulla oblongata failed to reveal any histopathologic studies. The few instances of thrombosis of the spinal artery in the lower cervical region that were reported have no bearing on this study. In this presentation, the syndromes of the vertebral artery, with special emphasis on the syndrome of the anterior spinal artery of the medulla oblongata, will be discussed. A brief description of the anatomic distribution of these two vessels will elucidate the problem.

DESCRIPTION OF THE VERTEBRAL ARTERY

The vertebral artery arises from the upper and posterior part of the subclavian artery between the scalenus anterior and longus colli muscles. For purposes of description it is divided into four parts, the first three of which are outside the cranial cavity and give rise to muscular branches.

The fourth part enters the vertebral canal, pierces the dura and runs upward into the cranial cavity. It lodges between the roots of the hypoglossal nerve posteriorly and the first dentation of the ligamentum denticulatum anteriorly, pierces the arachnoid, passes gradually upward and inward to the front of the medulla oblongata and reaches the lower border of the ventral surface of the pons, where it unites with its fellow of the opposite side to form the basilar artery. During its course in the posterior fossa it gives off the following branches:

1. Meningeal branches. These supply the respective parts of the meninges of the medulla oblongata.

2. Posterior spinal artery. This slender artery arises more commonly from the posterior inferior cerebellar artery; occasionally it arises from the vertebral artery directly. The artery runs downward on the side of the medulla oblongata. It supplies brances to the pia mater and forms a more or less regular anastomosis with its fellow of the opposite side on the medial and lateral aspects of the posterior nerve roots, and ends by joining the anterior spinal artery.

3. Anterior spinal artery. This arises about 0.75 to 1 cm. from the termination of the vertebral artery and runs obliquely downward and inward in front of the medulla oblongata to unite with its fellow of the opposite side, forming the single anterior spinal artery which descends along the anterior median fissure of the medulla oblongata and spinal cord (fig. 1). It is reenforced by anastomosing branches from the vertebral, intercostal and lumbar arteries. It supplies branches to the pia mater and spinal cord, and unites below with the posterior spinal arteries. Anomalies of the anterior spinal arteries of the medulla oblongata have been observed. These may arise at the point of union

of the two vertebral arteries. The left anterior spinal artery is frequently larger, and the right may be absent. Spiller [2] noted that these two vessels sometimes descend several centimeters before uniting; at other times they unite to form one vessel shortly beyond their origin. He also observed complete absence of the right vertebral and anterior spinal arteries.

The anterior spinal arteries of the medulla oblongata supply, in sections of the medulla oblongata through the tenth, eleventh and twelfth nerve nuclei, the pyramids, the medial lemnisci and occasionally the fibers of the hypoglossal nerves and the ventrolateral parts of the

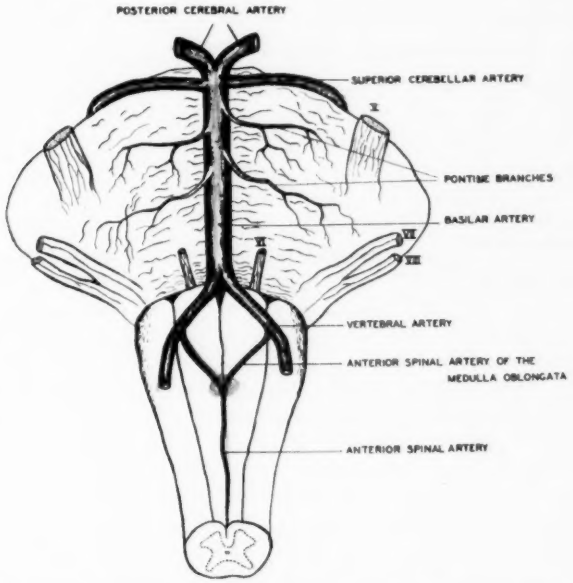

Fig. 1.—Diagram illustrating the vascular supply of the medulla oblongata by the vertebral and the anterior spinal arteries.

inferior olivary nuclei. Spiller was of the opinion that the hypoglossal nerve, as well as the vago-accessory nerve, is nourished by the vertebral artery. According to Duret,[3] branches of the anterior spinal artery may also supply the interolivary bundles, the posterior longitudinal bundle, the hypoglossal nuclei and other nuclei below the fourth ventricle.

As pointed out in a previous communication,[1b] the lateral part of the medulla oblongata from the inferior olivary nucleus to the corpus

2. Spiller, W. G.: The Symptom Complex of a Lesion of the Uppermost Portion of the Anterior Spinal and Adjoining Portion of the Vertebral Arteries, J. Nerv. & Ment. Dis. **35**:775, 1908.

3. Duret: Sur la distribution des artères nouricières du bulbe rachidien, Ann. de phys. norm. **5**:97, 1873.

restiforme is nourished by the posterior inferior cerebellar artery. At times branches of the posterior inferior cerebellar artery supplying the medulla oblongata may be replaced by direct branches from the vertebral artery. Foix, Hillemand and Schalet [4] believed that this part of the medulla oblongata is supplied by the lateral artery of the medulla oblongata, a branch of the basilar or of the vertebral artery. Most observers have believed that the inferior olivary nuclei at this level are supplied by lateral branches of the vertebral arteries. In some of the cases which I have observed, destruction of the posterolateral parts of the inferior olivary nuclei followed thrombosis of the posterior inferior cerebellar artery. In one of the cases to be reported it was demonstrated that the ventral part of the inferior olivary nucleus was supplied by the anterior spinal artery.

4. Posterior inferior cerebellar artery. This was discussed in a previous communication.[1b]

METHOD OF PROCEDURE

Sections of the involved medulla oblongata, as well as sections above and below the lesions, were embedded in pyroxylin (celloidin), cut serially and stained by myelin sheath and cresyl violet methods.

REPORT OF CASES

CASE 1.—*Occlusion of the right anterior spinal artery of the medulla oblongata with ipsilateral destruction of the pyramid, the medial lemniscus, the posterior longitudinal bundle and the ventrolateral part of the inferior olivary nucleus. Contralateral pyramidal tract signs, loss in discriminative sensibility and nystagmus. The other neurologic signs present were due to occlusion of the right vertebral and branches of the basilar artery.*

History.—R. L., a woman aged 54, was admitted to this hospital on Feb. 11, 1933. During a theatrical performance on Jan. 1, 1933, she experienced a peculiar feeling of numbness on the left side of the body and could not use the left arm or leg. Previous to this episode she had had frequent attacks of vertigo, headaches and dizziness. Her father and a maternal aunt had had diabetes; the father died at the age of 45 of a "stroke."

At the age of 29 the patient contracted gonorrhea from her husband. The first and only pregnancy terminated in a spontaneous abortion at three and one-half months. She stated that there had been no syphilitic infection. In 1920 diabetes and hypertension were diagnosed. In 1928 she had a transitory attack of "amaurosis," from which she recovered on the same day, after venesection and administration of insulin. While riding in a taxicab in 1931 she received an injury to the forehead. Roentgen examination of the skull gave negative results.

General Examination.—The patient was poorly nourished and bedridden, with a slight yellowish tinge to the skin, enlargement of the heart to the left, sclerosis of the radial arteries and a blood pressure of 190 systolic and 110 diastolic.

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4. Foix, C. L.; Hillemand, P., and Schalet, I.: Sur le syndrome latéral du bulbe supérieur, Rev. neurol. **32**:160, 1925.

Neurologic Examination.—There were: left flaccid hemiparesis, with increased deep reflexes, absence of abdominal reflexes, and Babinski, Chaddock and Rossolimo signs on the same side; complete loss of vibratory sensation on the left side of the body and marked impairment of position sense in the left toes, fingers and wrist; astereognosis and loss in two point discrimination on the left side of the body; hyperpathia in the left hand and ankle; old partial occlusion of the left central retinal artery, with atrophy of the left disk and retinal arteriosclerosis; constriction of the left visual field; slightly irregular pupils, the left reacting poorly to light but well in accommodation; paralysis of the right external rectus muscle, with bilateral impairment of lateral conjugate deviation, which was more marked to the right; poor convergence; widening of the right palpebral fissure; coarse nystagmus to the left, and occasional nystagmus on upward gaze; complete right nuclear facial paralysis; negative Bárány tests; deviation of the tongue to the left, with some questionable fibrillations on the left, and incontinence of urine and feces.

Mental Examination.—The patient was unstable and emotional, alternating rapidly between noisy tears and loud laughter. There were no other mental symptoms.

Course.—During the period of hospitalization there were episodes of hyperglycemia, with marked mental changes, drowsiness, confusion and disorientation. Occasionally there was marked glycosuria; at one time the blood sugar was as high as 389 mg. per hundred cubic centimeters. Urine concentration tests in February and October 1933 showed fixation of the specific gravity between 1.015 and 1.018. Bronchopneumonia developed, and the patient died on December 6.

Laboratory Data.—Chemical study of the blood disclosed: blood sugar, between 178 and 390 mg. per hundred cubic centimeters; urea nitrogen, 13.9 mg.; cholesterol, 185 mg. The Wassermann reaction of the blood was negative. The serologic reaction of the spinal fluid and manometric readings were normal. The urine contained a faint trace of albumin, and sugar was present.

Clinical and Anatomic Diagnoses.—The following diagnosis was made: thrombosis of the uppermost part of the right anterior spinal artery; partial thrombosis of the vertebral artery, of the pontile branches of the basilar artery and of the lenticulostriate and left central retinal arteries; generalized and cerebral arteriosclerosis, and diabetes mellitus.

Autopsy.—Gross Examination: The cerebral convolutions were slightly atrophied. All vessels at the base contained numerous atheromatous plaques. The anterior inferior cerebellar arteries were very small. A thrombus partially occluded the right vertebral artery; it extended into the right anterior spinal artery, obstructing it completely. At its origin the basilar artery was also partially occluded. The medulla oblongata appeared smaller than normal. The brain was cut coronally. In the distribution of the right lenticulostriate artery, an area of softening replaced by a cyst had destroyed the caudate nucleus, part of the internal capsule, the putamen and the globus pallidus. On the right side the medulla oblongata was shrunken and atrophic; the inferior olivary nucleus appeared atrophied. There was a small area of softening in the brain stem, in the region of the right medial lemniscus, which extended as far as the sixth and seventh nerve nuclei. Sections of the medulla oblongata and pons were embedded in pyroxylin and cut serially. The spinal cord appeared normal.

Microscopic Examination: Sections of the pons through the superior part of the fourth ventricle disclosed an area of demyelinization of the lower parts of the right pyramid. The right median fillet was slightly demyelinated.

Sections of the medulla oblongata through the sixth and seventh nerve nuclei revealed an area of destruction involving the following structures on the right: the pyramid, the medial lemniscus, the posterior longitudinal bundle, the thalamo-olivary tract, and the sixth and seventh nerve nuclei (fig. 2). The right vertebral and the basilar artery at this level showed marked atherosclerotic changes.

Sections of the medulla oblongata through the ninth nerve nuclei disclosed an area of demyelinization on the right with destruction of the pyramid, the medial lemniscus, the tectospinal tract and the posterior longitudinal bundle, and partial demyelinization of the periolivary and hilar fibers on the ventrolateral aspect of the right inferior olivary nucleus (fig. 3). The ventrolateral portion of the thalamo-olivary bundle took the myelin stain poorly (fig. 3). The left corpus restiforme was reduced in size and the left pyramid was slightly demyelinated (fig. 3).

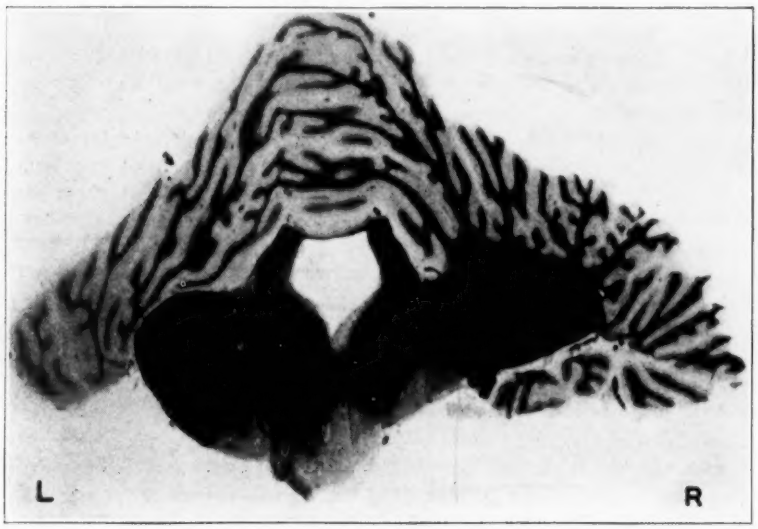

Fig. 2.—Section of the brain stem at the level of the sixth and seventh nerve nuclei. Notice the demyelinization of the right pyramid, medial lemniscus and posterior longitudinal bundle. Myelin sheath stain.

In sections of the medulla oblongata through the tenth and twelfth cranial nerve nuclei, except for the sparing of the right posterior longitudinal bundle and the tectospinal tract, there was involvement of the same structures (fig. 4). The right hypoglossal nucleus and nerve appeared normal. The left corpus restiforme appeared atrophied (fig. 4) as a result of the lesion in the right inferior olivary nucleus.

Sections through the crossing of the lemnisci and pyramids revealed demyelinization of the right pyramid. The right medial lemniscus and Helweg's tract at this level were only slightly involved (fig. 5). In cresyl violet preparations, the areas of destruction were filled with astrocytes, *gemästete* glia cells and compound granular corpuscles. The nerve cells of the ventral portion of the inferior olivary nucleus showed all types of pathologic changes: retrograde degeneration, pseudo-hypertrophy and vacuolation. The right anterior spinal and adjacent vertebral

arteries revealed marked thickening and proliferation of the intima, foam cells, splitting of the lamina elastica and slight calcification of the media.

Sections of the spinal cord showed descending demyelinization of the left crossed pyramidal tract.

Comment.—The contralateral pyramidal tract signs and discriminative sensory disturbances present in the patient were the result of an

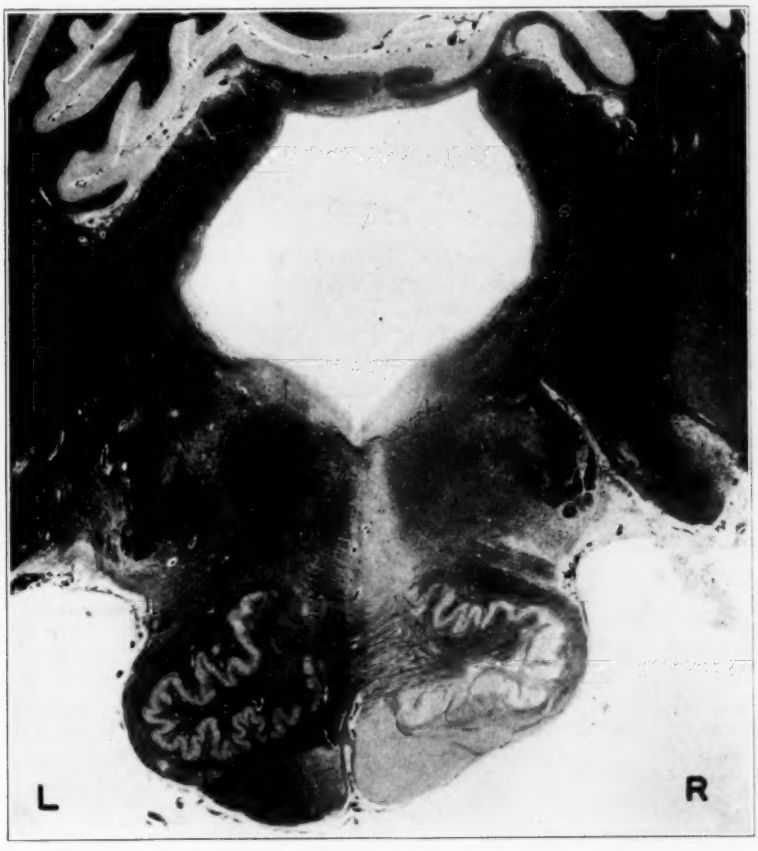

Fig. 3.—Section of the medulla oblongata through the brachium conjunctivum and eighth and ninth nerve nuclei showing demyelinization of the right pyramid, medial lemniscus, tectospinal tract and posterior longitudinal bundle, and marked pallor of the ventrolateral part of the right inferior olivary nucleus and partial destruction of the olivodentate fibers. Notice the slight atrophy of the opposite corpus restiforme. Myelin sheath stain.

occlusion of part of the right anterior spinal artery supplying the medulla oblongata. Although there were questionable fibrillations of the right side of the tongue, the hypoglossal nucleus and its nerve showed no

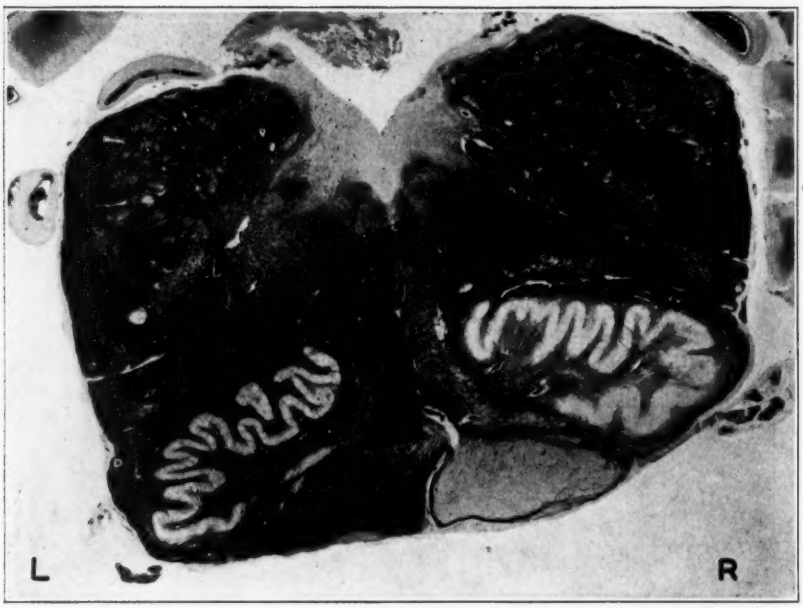

Fig. 4.—Section of the medulla oblongata through the tenth and twelfth nerve nuclei showing an area of demyelinization on the right with destruction of the pyramid and medial lemniscus. The posterior longitudinal bundle at this level was spared. The hypoglossal nerve was intact. The opposite corpus restiforme was atrophied. Part of the right thalamo-olivary bundle and of the perioolivary and hilar fibers of the ventrolateral part of the inferior olivary nucleus were partially demyelinated. Myelin sheath stain.

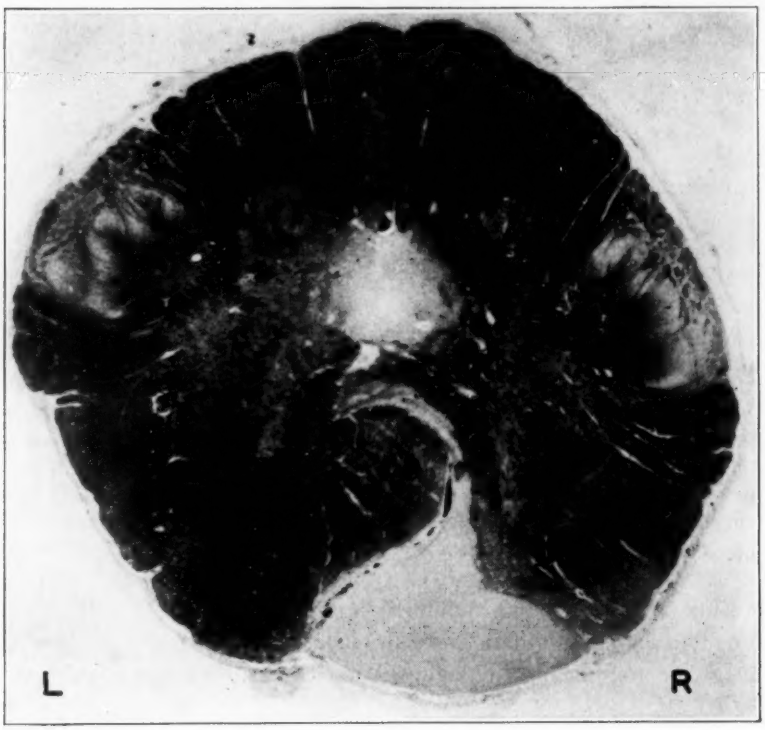

Fig. 5.—Section passing through the crossing of the pyramids, showing demyelinization of the right pyramid and slight destruction of the fibers of the right medial lemniscus and of Helweg's tract. Myelin sheath stain.

pathologic changes. In addition to the typical syndrome of the anterior spinal artery of the medulla oblongata, there were other neurologic findings, which were caused by partial occlusion of the right vertebral artery and of branches of the basilar artery. The paralysis of lateral gaze and of the right external rectus muscle and the nuclear facial palsy were undoubtedly caused by involvement of the respective structures by disease of the vertebral and of branches of the basilar artery. The nystagmus may have been the result of occlusion of the anterior spinal artery, since in this case this vessel supplied the posterior longitudinal bundle (fig. 3). The impairment of the associated eye movements to the left was caused possibly by involvement of the para-abducens nucleus or of the oculogyric and cephalogyric aberrant pyramidal fibers. Of interest was the left flaccid hemiplegia as a result of complete destruction of the right pyramid in the medulla oblongata. According to Kennard and Fulton,[5] flaccid hemiplegia occurs when the motor fibers of area 4 alone are involved. In this case the entire right pyramid in the medulla oblongata was affected, thus implicating both the premotor and motor fibers at this level. Perhaps the combined lesions of the medial lemniscus and pyramid offer the explanation for the flaccid hemiplegia. As others have emphasized, flaccid hemiplegia is not uncommon in combined lesions of the motor area and parietal lobe. Another interesting feature was the involvement of the ventral part of the inferior olivary nucleus. This part of the olivary nucleus is occasionally supplied by the anterior spinal artery of the medulla oblongata.

CASE 2.—*Occlusion of the left anterior spinal artery of the medulla oblongata with bilateral destruction of the pyramids and ipsilateral involvement of the medial lemniscus and posterior longitudinal bundle. Bilateral pyramidal tract signs, more marked on the right, contralateral loss in discriminative sensation, and nystagmus. The other neurologic signs present were due to involvement of branches of the left posterior inferior cerebellar artery.*

History.—S. K., a man aged 40, was admitted to this hospital on April 27, 1933, with a history of repeated cramplike pains in the feet and calf muscles since 1929, most pronounced on walking and relieved by rest. In 1930 the patient had a mild coronary attack followed by a similar but severe attack in September 1931. Since then he frequently complained of precordial pain radiating to the left shoulder, along the medial aspect of the left arm and hand, and epigastric distress after meals. In January 1932 he experienced first a feeling of constriction in the chest and later had an episode of hiccup which lasted nine days and an episode of vomiting which lasted three days. In February 1932 he had an attack of severe pain in the right upper extremity and right side of the face, followed by transitory numbness of the right side of the body and inability to move the right extremities.

5. Kennard, M. A., and Fulton, J. F.: The Localizing Significance of Spasticity, Reflex Grasping and the Signs of Babinski and Rossolimo, Brain **56**:213, 1933.

Four days later he had urinary and fecal incontinence and difficulty in talking. Soon after, speech returned and the incontinence disappeared. The past history was without significance except for pneumonia in 1911, which was complicated by empyema, for which resection of a rib was performed.

General Examination.—There were: a scar of the previous rib resection in the right lower part of the chest posteriorly; diminished expansion of the right side of the chest; signs of consolidation and moisture over the area of the old empyema, and exaggerated vesicular breathing over the left side of the chest, with coarse râles at the left base; slight cardiac enlargement and a blood pressure of 120 systolic and 95 diastolic.

Neurologic Examination.—There were: slight ataxia on the left with the finger-to-nose and heel-to-knee tests; right spastic hemiplegia, with increased deep reflexes, inexhaustible ankle and patellar clonus, diminished abdominal reflexes and Babinski, Chaddock and Rossolimo signs on the same side; slight pyramidal tract signs on the opposite side; moderate atrophy of the smaller intrinsic muscles of the right hand and of the muscles of the arm, thigh and leg. There were questionable right hypesthesia, hypalgesia and hypothermesthesia; marked impairment of vibratory sensation on the right side of the body and of position sense in the right toes and fingers; impairment of two point discrimination on the right; astereognosis of the right hand, and severe "spontaneous pain" when the right upper extremity was flexed or extended. The fundi were normal. The right pupil was slightly larger than the left, but both reacted to light and in accommodation. Convergence was slightly impaired on the right. The left palpebral fissure appeared somewhat smaller than the right. The gag reflex was absent on the left, but voluntary movements of the palate and pharynx were normal. There was no atrophy or fibrillations of the tongue. Speech was slow and had a nasal quality. The skin of the right hand and fingers was cool and clammy; the nails on the same side were cyanotic and contained raised longitudinal grooves. There were urinary and fecal incontinence.

Mental Examination.—This gave negative results.

Course.—Shortly after admission to the hospital the patient had a cerebrovascular insult, followed by transient left hemiplegia. During his stay he had frequent attacks of precordial and epigastric pain and subjective painful sensations in the right extremities; the pains were not relieved by vasodilators, but only by sedatives. He had frequent changes in respiratory rate and rhythm; these were considered to be due to involvement of the respiratory center. During the last few months, epidural injections of procaine hydrochloride and 95 per cent alcohol were administered for the severe painful sensations, resulting only in moderate relief. The patient continued to complain of excruciating pains on the right side and died suddenly on Jan. 6, 1934, during an attack of coronary occlusion.

Laboratory Data.—The results of urinalysis, the blood cell counts, and the results of chemical and serologic examination of the blood were normal. Electrocardiographic tracings disclosed a left ventricular preponderance and intraventricular conduction disturbance. Roentgen examination of the chest showed moderate cardiac enlargement and small areas of consolidation scattered throughout the lower lobes, due to the old empyema.

Clinical and Anatomic Diagnoses.—The following diagnosis was made: thrombosis of the upper part of the left anterior spinal artery and of branches of the left posterior inferior cerebellar artery; cerebrovascular disease, with thrombosis of the temporal and posterior parietal branches of the right middle cerebral artery; coronary thrombosis with multiple myocardial infarctions.

Autopsy.—Gross Examination: There was an area of softening along the right sylvian fissure, involving the first temporal convolution, the supramarginal and the angular gyri. The brain was cut coronally. The softening extended slightly into the external capsule and into the putamen.

Microscopic Examination: Coronal sections through the third ventricle stained by the myelin sheath method showed destruction of the right superior temporal convolution, part of the island of Reil, the external capsule, the claustrum and the putamen. The white matter in the centrum ovale stained poorly. The

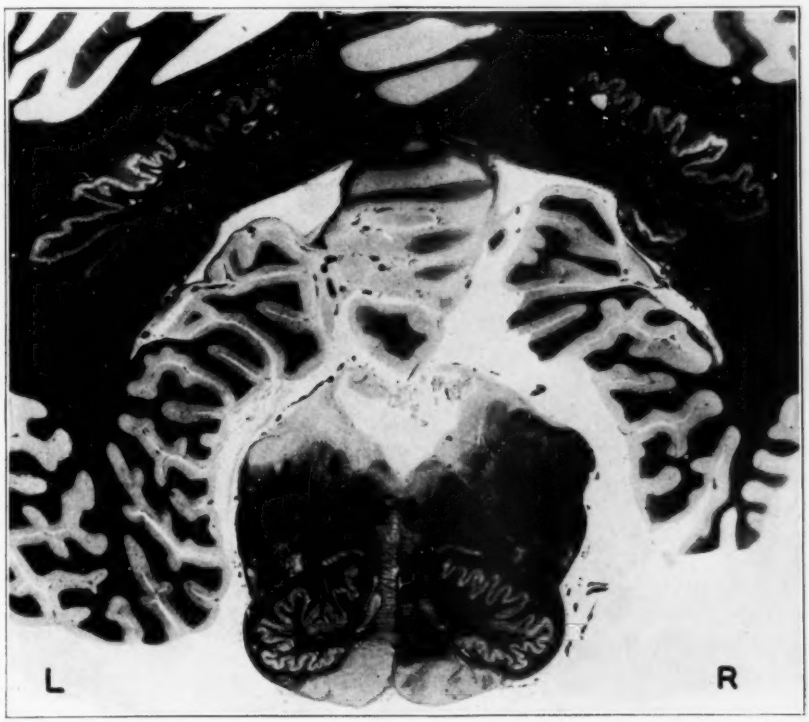

Fig. 6.—Section of the medulla oblongata through the tenth nerve nucleus, showing demyelinization of both pyramids, the left more than the right, the left medial lemniscus, tectospinal tract and part of the posterior longitudinal bundle. The left nucleus vestibularis medialis and the corpus restiforme were also partially destroyed. Myelin sheath stain.

right caudate nucleus was shrunken. The vessels in these areas showed atherosclerotic changes.

In sections passing through the red nucleus the cerebral peduncles appeared normal, and in sections of the pons the pyramids were not demyelinated.

Sections of the medulla oblongata through the tenth nerve nuclei showed: demyelinization of both pyramids, the left more than the right; demyelinization of the left medial lemniscus, tectospinal tract and posterior longitudinal bundle; partial destruction of the nucleus vestibularis medialis, corpus restiforme and part of the nucleus and tractus solitarius on the left side (fig. 6). The interolivary

and hilar fibers in this region were not demyelinated (fig. 6). With a higher magnification the fibers of the left pyramid were seen to be completely destroyed; those of the right pyramid were partially disintegrated. The inferior part of the medial lemniscus was more involved than the superior part. A few myelinated fibers could still be seen in the upper third of the medial lemniscus; this was best seen in sections below this level. Slight demyelinization of a few fibers of the right medial lemniscus was also noted. In cresyl violet preparations the areas of demyelinization of the pyramid, medial lemniscus and tectospinal tract were replaced by proliferating astrocytes. The medial and spinal vestibular nuclei, part

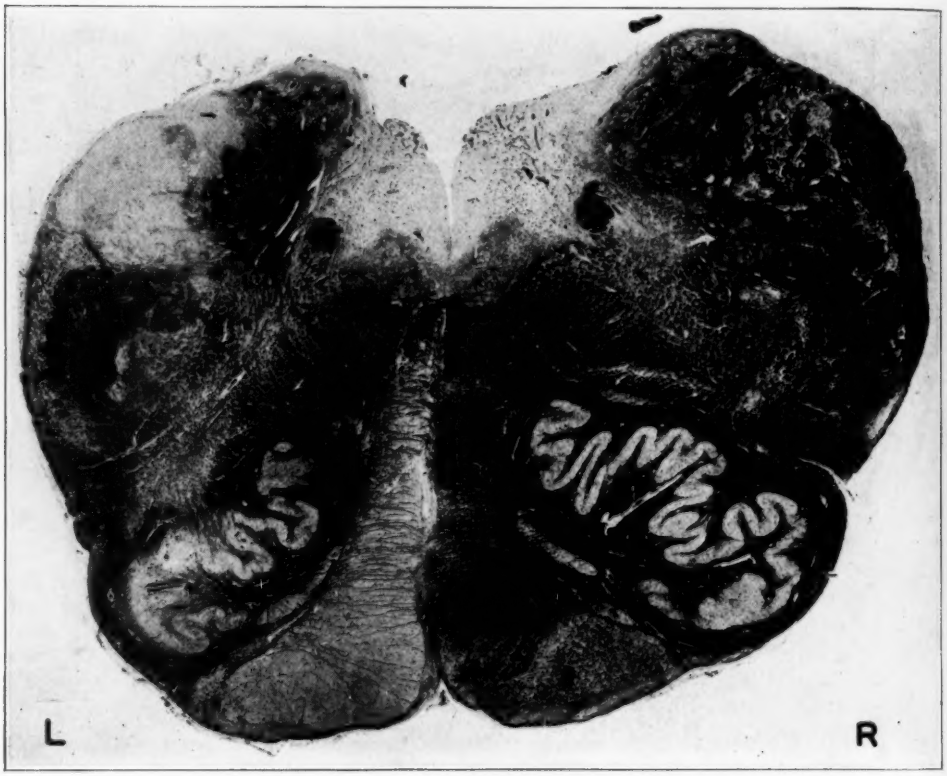

Fig. 7.—Section of the medulla oblongata passing through the beginning of the nuclei cuneati showing involvement of both pyramids and left medial lemniscus; a few of the fibers of the right medial lemniscus are also slightly demyelinated. The posterior longitudinal bundle was spared at this level. The involvement of the left corpus restiforme, part of the left nucleus cuneatus, nucleus ambiguus, nuclei lateralis and inferior olivary nucleus was the result of the lesion of branches of the left posterior inferior cerebellar artery. Myelin sheath stain.

of the tractus and nucleus solitarius and the nucleus ambiguus on the left side were filled with numerous glia cells, mostly astrocytes, and with compound granular corpuscles. A few glia cells were also found within the region of the left spinothalamic tract. The various ganglion cells in the areas of degeneration, especially those of the vestibular nuclei, showed all kinds of pathologic changes.

In sections of the medulla oblongata passing through the beginning of the nucleus cuneatus, except for sparing of the posterior longitudinal bundle, there was involvement of the same structures as in the previous section. At this level the left corpus restiforme and the nucleus ambiguus were more extensively implicated than in sections above it (figs. 7 and 8). In addition, the left nucleus cuneatus and the nuclei laterales were partially destroyed; the dorsolateral part of the left olivary nucleus was shrunken and contained a small cyst in which there were compound granular corpuscles, astrocytes and proliferated vessels. The ganglion cells within this cystic area showed various pathologic changes, and the olivary vessels were markedly atherosclerotic. The left thalamo-olivary bundle

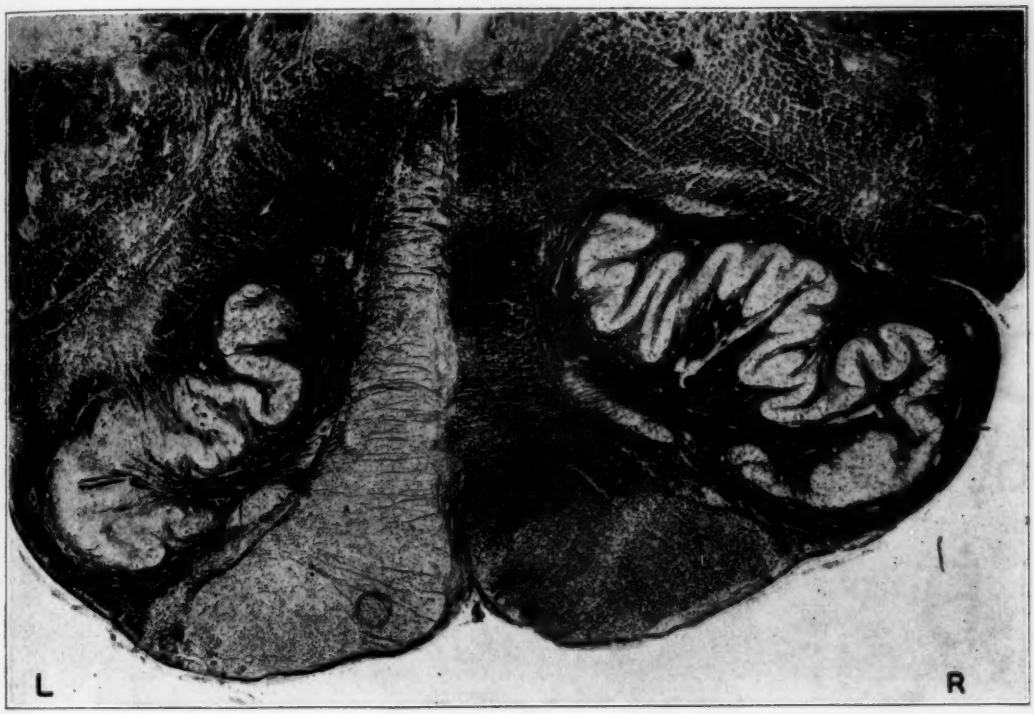

Fig. 8.—Same section as in figure 7, enlarged, revealing preservation of the left posterior longitudinal bundle and the left hypoglossal nerve at this level. The small cyst of the dorsolateral part of the left olivary nucleus, the degeneration of the nuclei lateralis and the poorly stained left thalamo-olivary fibers can best be seen at this level. Myelin sheath stain.

stained poorly as compared with the right (fig. 8). The ganglion cells of the nucleus ambiguus and nucleus and tractus solitarius at this level were decreased in number and were devoid of chromatin. The nerve cells of the hypoglossal nucleus were well preserved. Within the nucleus cuneatus there were collections of compound granular corpuscles and astrocytes, and the ganglion cells showed retrograde degeneration.

In sections through the crossing of the lemnisci and pyramids there was demyelinization of both pyramids, the left more than the right, and of part of the

raphe (fig. 9). In cresyl violet preparations the left pyramid and the medial lemniscus were filled with numerous astrocytes and glia cells. The ganglion cells of the eleventh and twelfth nerve nuclei and the ventral cerebellar tracts were intact.

In sections through the spinal cord there was descending degeneration of both crossed and of the left uncrossed pyramidal tracts; the left pyramidal tract was more involved than the right.

Comment.—The original symptoms—right pyramidal tract signs and discriminative sensory disturbances—were accounted for by the

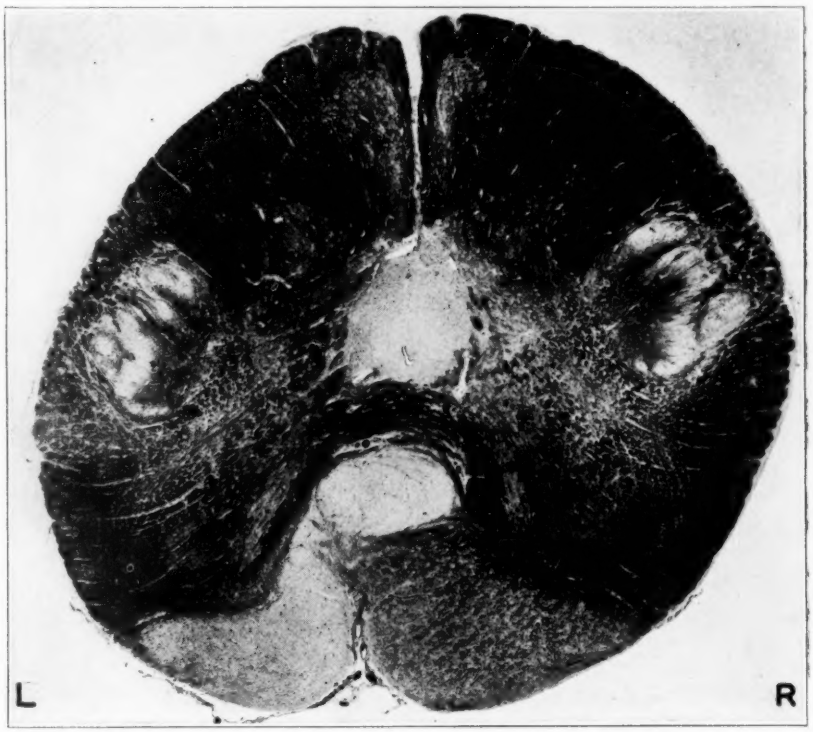

Fig. 9.—Section through the crossing of the lemnisci and pyramids showing demyelinization of both pyramids, the left more than the right, and of part of the fibers of the raphe. Myelin sheath stain.

occlusion of the anterior spinal artery of the medulla oblongata as a result of destruction of the left pyramid and medial lemniscus. The nystagmus may also have been caused by the partial destruction of the left posterior longitudinal bundle, which may be supplied at this level by the anterior spinal artery. The other symptoms—vomiting, hiccup, dysphagia and dysarthria—were produced by lesions of the smaller branches of the left posterior inferior cerebellar artery, which supplies

the nucleus ambiguus, the nucleus and tractus solitarius and the vestibular nuclei. The left cerebellar signs were due to involvement of the left corpus restiforme (fig. 7) as a result of implication of a branch of the left posterior inferior cerebellar artery. The mild and questionable right spinothalamic sensory disturbances may have been due to partial involvement of the left spinothalamic tract resulting from occlusion of a branch of the left posterior inferior cerebellar artery. The hyperaffectivity on the right side probably resulted from irritation of the spinothalamic pathways on the left. The left transient hemiplegia was secondary to the edema following the occlusion of the temporal and parietal branches of the right middle cerebral artery.

CLINICAL AND ANATOMIC CONSIDERATIONS

On the basis of clinical observations, Spiller,[2] in 1908, was the first to postulate the syndrome resulting from occlusion of the uppermost portion of the anterior spinal artery. He stated that

> the area of supply of the upper part of the anterior spinal arteries is chiefly the anterior and middle portions of the medulla oblongata. Occlusion of these arteries or hemorrhage from them, including the adjoining part of the vertebral arteries, should therefore give a very definite symptom group. This may be unilateral or bilateral, depending on the union of the two arteries near their origin or several centimeters below. As these arteries are side by side shortly below their origin, even when they do not at once unite, the symptom complex is likely to be bilateral.

As his reported case clearly showed, he predicted paralysis of all the extremities, trunk and neck, with sparing of the facial musculature, and disturbances of sensation due to a lesion of the medial lemniscus. The tongue, he believed, should escape,

> as the hypoglossus nerve has at least a portion of its origin above the origin of the anterior spinal arteries, but it might be involved by implication of the vertebrals.

The two case histories forming part of this contribution show conclusively that Spiller's formulation was correct. At the time, Spiller was somewhat skeptical that the symptoms could be unilateral, as both the pyramidal and the lemniscus fibers decussate at about the same level. In these two cases, however, the main symptoms were unilateral. As Spiller predicted, the hypoglossal nerve and nucleus were spared in both instances. Since Spiller's report, a number of less clearcut clinical instances of the syndrome of the anterior spinal artery have been recorded, but so far histopathologic reports have not been published.

Analysis of the two cases under discussion reveals that the onset and the type of symptoms were about the same in both. The patients experienced a feeling of numbness and diminution in motor power contralateral to the side of the lesion. As already stated, the neurologic findings consisted of contralateral pyramidal tract signs and loss of

discriminative sensations. In the first case questionable ipsilateral fibrillations of the tongue were recorded, but the nerve cells of the hypoglossal nucleus and the fibers of the hypoglossal nerve were intact. In addition to these findings, nystagmus was present in both instances; this symptom was most likely caused by lesions of the posterior longitudinal bundle. At certain levels of the medulla oblongata this structure, as seen in the histopathologic preparations (figs. 3 and 6), was supplied by the uppermost part of the anterior spinal artery.

Anatomically, the following structures of the medulla oblongata at levels between the tenth and twelfth nerve nuclei were found implicated as a result of obstruction of the anterior spinal artery: the pyramid, the medial lemniscus, the posterior longitudinal bundle and the tectospinal tract. In case 1 there was also involvement of the ventrolateral part of the inferior olivary nucleus and its fiber connections (figs. 3 and 4). Symptoms referable to lesions of the inferior olivary nucleus, such as myoclonus, rigidity, and speech and postural disturbances, were not recorded in these two cases. The lesion in the olivary nucleus confirms Duret's [3] opinion that the anterior spinal artery supplies part of this structure. The absence of such a lesion in case 2, except for the small area of destruction of the dorsolateral part as a result of occlusion of a branch of the posterior inferior cerebellar artery, is an indication that the vascular distribution of the anterior spinal artery may vary. In both cases the opposite pyramid was also involved, only slightly in case 1 and more so in case 2. The involvement of both pyramids in case 2 confirms Spiller's view that bilateral involvement may occur, especially if the two arteries unite close to their origin instead of several centimeters below. In this case, however, the opposite medial lemniscus was intact. The urinary and fecal incontinence present in both cases may have been due to the involvement of both pyramids.

A symptom which was present in both instances and which deserves consideration was contralateral "spontaneous pain." In case 2 the "spontaneous pain" was probably due to the incomplete destruction of the left spinothalamic tract as a result of occlusion of a branch of the posterior inferior cerebellar artery. In case 1 the spinothalamic tract was intact and the explanation becomes more difficult, unless one accepts Foerster's contention that visceral pain fibers are present in the posterior columns and the medial lemniscus.

A number of other neurologic signs were found in both instances which were the result of implication of other vessels. In case 1, because of the presence of a thrombus in the right vertebral artery and of atherosclerotic changes in some of the pontile branches of the basilar artery there was also involvement of the sixth and seventh nerves on the ipsilateral side. In case 2, as a result of lesions of the branches of the

left posterior inferior cerebellar artery there were also present ipsilateral cerebellar signs, speech disturbances and respiratory difficulties. As shown in these two cases, clinical diagnosis of occlusion of the anterior spinal artery becomes difficult when there is involvement of other vessels, especially of the posterior inferior cerebellar and the vertebral arteries.

SUMMARY AND CONCLUSIONS

Two cases of occlusion of the uppermost portion of the anterior spinal artery are presented. In both instances there was ipsilateral destruction of the pyramid, medial lemniscus, posterior longitudinal bundle and tectospinal tract. The ventrolateral part of the ipsilateral inferior olivary nucleus in case 1 was also involved. The contralateral pyramid was slightly affected in case 1 and markedly in case 2. The hypoglossal nucleus and nerve were spared in both instances.

Clinically, both cases showed contralateral pyramidal tract signs and loss of discriminative sensibility; nystagmus and urinary and fecal incontinence were also present. Atrophy of the tongue was not recorded in either case, although questionable fibrillations of the tongue were noted in case 1.

Case Reports

PORENCEPHALY: DIAGNOSIS AND TREATMENT

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PHILADELPHIA

Porencephaly is a neurologic entity capable of clinical diagnosis. Since Heschl's [1] publication in 1859, the subject has been viewed largely from the standpoint of the gross and microscopic pathologic characteristics and pathogenesis and has received scant clinical and therapeutic attention. In a search for the causes and means of relief of convulsive states our attention was directed to a group of nine persons in whom the features distinguishing the condition from idiopathic or essential epilepsy were the presence of organic neurologic signs and focal seizures and the absence of evidence of increased intracranial pressure. In all cases there was evidence of a neurologic abnormality existing since early childhood, except in one instance in which a later trauma was the unquestioned etiologic factor. Study of these cases enabled us to make a tentative clinical diagnosis of porencephaly. This was confirmed subsequently by encephalographic studies, and relief was obtained in a large proportion of instances by proper surgical procedures.

In this paper we employ the term porencephaly to signify a defect in the cerebral or cerebellar structure appearing as a cystlike cavity communicating with the ventricles or separated from them only by a thin layer of brain tissue, covered on the outside by the pia-arachnoid and filled with a clear, colorless fluid (LeCount and Semerak [2]). This definition is stressed because of the confusion regarding the concept of porencephaly in the literature. Thus, Bourneville and Schwartz [3] differentiated between true and false porencephaly, the former induced by disease of intra-uterine or extra-uterine life and the latter by disturbances of circulation. Obersteiner [4] designated any porus in the brain which does not communicate with the ventricle as pseudoporen-

* Dr. Patten died on June 2, 1936.

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1. Heschl, R.: Gehirndefekt und Hydrocephalus, Vrtljschr. f. d. prakt. Heilk. (*a*) **61**:59, 1859; (*b*) **72**:102, 1861; (*c*) **100**:40, 1868.

2. LeCount, E. R., and Semerak, C. B.: Porencephaly, Arch. Neurol. & Psychiat. **14**:365 (Sept.) 1925.

3. Bourneville and Schwartz: Nouvelle contribution à l'étude de la pseudoporencéphalie et de la porencéphalie vraie, Progrès méd. **8**:169 and 201, 1898.

4. Obersteiner, H.: Anleitung beim Studium des Baues der nervösen Zentralorgane im gesunden und kranken Zustände, ed. 5, Vienna, Franz Deuticke, 1912, vol. 19, p. 68.

cephaly. Kundrat [5] applied the term porencephaly to any defect roofed over by the arachnoid. Von Kahlden [6] restricted the name porencephaly to such defects as are acquired during intra-uterine life and not due to trauma. Siegmund,[7] on the other hand, combined under the term porencephaly all defects due to destruction unaccompanied by infection. A careful review of the literature revealed that it is advisable to employ the term porencephaly on the basis of actual anatomic structures rather than on etiologic considerations.

ANALYSIS OF CASES

An analysis of the nine cases follows. Detailed observations are mentioned in the report of the cases, and a table giving a summary is presented.

The actual problem presented in each case was the relief or cure of convulsive seizures, although in no instance did the patient make serious objection to the physical or neurologic handicaps. Most of the patients had received treatment for seizures. The usual methods of therapy, including dehydration procedures in some cases, had been applied, without effect. Since the condition is basically cystic, it might be assumed that by lessening the contents of the cyst through dehydration the patient should have been relieved of the convulsive phenomena, but this did not occur. Similarly, phenobarbital, which with the use of bromides usually affords some relief in cases of essential epilepsy, had little effect in these cases.

1. *Age and Sex Incidence.*—The ages of the nine patients varied from 13 to 22 years. The average age was 16 plus. Little can be deduced regarding the age incidence from this small number of patients, in view of the fact that they came under observation chiefly because of a specific disability, the convulsive state. It is known that porencephaly may exist without any subjective symptoms and be discovered incidentally at autopsy. In this connection the figures of Schattenberg [8] on the incidence of death from porencephaly according to age are of interest: from birth to 1 year, twelve; from 1 to 10 years, eleven; from 10 to 20 years, fourteen; from 20 to 30 years, three; from 40 to 50 years, four, and from 50 to 60 years, two. Necropsy is not often performed, and therefore the frequency of porencephaly among persons living to old age may be greater than is generally supposed. It is of interest, however, that in most of the cases in our series death occurred between the ages of 10 and 20 years. Males predominated in the proportion of 2 to 1.

5. Kundrat, H.: Die Porencephalie, eine anatomische Studie, Graz, Leuschner & Lubensky, 1882.

6. von Kahlden, C.: Ueber Porencephalie, Beitr. z. path. Anat. u. z. allg. Path. **18**:231, 1895.

7. Siegmund, H.: Die Entstehung von Porencephalien und Sklerosen aus geburtstraumatischen Hirnschaedigungen, Virchows Arch. f. path. Anat. **241**:237, 1923.

8. Schattenberg, R.: Ueber einen umfangreichen porencephalischen Defekt des Gehirns bei einem Erwachsenen, Beitr. z. path. Anat. u. z. allg. Path. **5**:119, 1889.

Summary of Clinical Findings in Nine Cases of Porencephaly

Case No. Patient	Sex	Age, Yrs.	Birth Injuries	Postnatal Trauma or Infections Disease	Character of Early Development	Mental Development (Including Delinquency)	Abnormalities (Existing Since Early Life)	Convulsions—Age of Onset; Character (Motor, Sensory); Frequency; Loss of Consciousness	Motor Disturbances	Sensory Disturbances	Atrophy of Optic Nerve	Visual Field Defects	Roentgenographic Location of Cyst	Results of Surgical Treatment; Frequency of Convulsions
Case 1 J. H.	M	13	Difficult labor	.....	Did not talk until 3 yr. and 6 mo. of age	.....	Record not available	3 or 4 convulsions daily at monthly intervals; right jacksonian seizures at 11 yr.	Weakness of right hand	.....	.....	.....	Left frontal	Marked improvement; 2 attacks of dizziness; no loss of consciousness
Case 2 M. H.	F	18	.....	Injury through mouth at age of 3 yr.	Normal	.....	Lack of development of right extremities	2 convulsions a month; right jacksonian and generalized convulsions at 3 yr.	Right spastic hemiplegia	Right hemianesthesia	.....	.....	Left precentral	Convulsions ceased; improvement in power
Case 3 R. L.	F	15	.....	Cyanotic first week; convulsions first year	Normal	.....	Lack of development of right upper extremity	Right jacksonian and generalized convulsions every two months; onset at 11 yr., coincident with onset of menses	Right hemiparesis	.....	.....	Right hemianopia	Left occipitoparietal	Convulsions ceased
Case 4 S. B.	M	14	.....	Megalocephaly; diphtheria; convulsions at age of 2 yr.	Did not walk or talk until 5 yr. old	Retardation	Lack of development of right side; large head; equinovarus	4 or 5 convulsions daily; right jacksonian convulsions at 14 yr.	Right hemiparesis	.....	.....	.....	Left parietal	Improvement; only 1 convulsion since treatment
Case 5 M. T.	F	18	.....	.....	Normal	.....	Lack of development of right arm	Convulsions of undetermined frequency and type from birth to 9 yr.; right jacksonian epilepsy from 12 to 18 yrs., once weekly	Weakness of right side of face and arm	.....	.....	Right hemianopia	Left temporoparietal	Motor convulsions ceased; sensory attacks infrequent
Case 6 W. P.	M	18	.....	Undetermined infection at age of 3 yr.	Normal	Retardation; delinquency	Lack of development of left side of body	Generalized left jacksonian convulsions and left athetosis at 4 yr. frequency not recorded	Left hemiparesis	.....	.....	.....	Right frontoparietal	Improvement
Case 7 B. R.	M	14	.....	Convulsions first 7 days; diphtheria; ordinary blow on head	Normal	.....	Right equinovarus	Daily convulsions; right jacksonian and and generalized seizures at 12 yr.	Left central facial palsy	Right hemianesthesia	.....	Right hemianopia	Left posterioparietal	Death
Case 8 C. Z.	M	22	.....	Injury at age of 17 yr.	Normal	.....	.....	Weekly convulsions; right jacksonian and generalized seizures at 17 yr.	.....	.....	.....	.....	Left parietal	Death
Case 9 E. S.	M	20	.....	Infection at age of 4 yr., followed by hemiplegia	Normal	Retardation	Lack of development of right side of body	About 10 convulsions a month; right jacksonian seizures at 10 yr.	Right hemiparesis	Right hemianesthesia	.....	Right hemianopia	Left occipitoparietal	Improvement with administration of phenobarbital; convulsive attack every 2 mo.

2. *Etiologic Factors.*—Nothing of importance regarding the cause of porencephaly is revealed by this study. The mother of the patient in case 7 had influenza during pregnancy. Only one patient (case 5) had a birth injury; in another instance (case 1) there was difficult labor. In case 7 there were convulsions for the first seven days of life, and in case 3, cyanosis for the first week and convulsions for the first year. In case 5 the patient had jacksonian convulsions until the age of 9 years. In case 4 there were evidences of hydrocephalus at the age of 3 or 4 months.

Injuries to the head did not play a large rôle in the etiology: In case 7 there was a history of an ordinary blow on the head; in case 2, an injury through the roof of the mouth, which was immediately followed by paralysis, and in case 8, a serious injury at the age of 17 years.

No definite conclusions can be drawn regarding the rôle of infection in our group of cases. Diphtheria occurred in two instances (cases 4 and 7), a severe infection of undetermined nature at the age of 3 years in case 6 and a severe infection at the age of 4 years, followed by paralysis, in case 9. In two instances (cases 1 and 4) delay in walking and talking was marked, and in three (cases 4, 6 and 9) there was definite retardation in mental development.

A review of the voluminous literature, which was best summarized by LeCount and Semerak,[2] is inconclusive regarding the etiology of this condition. With few exceptions, there is general agreement that porencephaly may be congenital or acquired. Among special causes mentioned in cases of congenital origin are defects of fetal development (Heschl [1]), disturbances of nutrition in the mother, anomalies of placental development and forceful contractions of the uterus, producing ischemia. The following causes were said to be common factors in cases both of the congenital and of the acquired type: (*a*) circulatory disturbances, including hemorrhage, embolism and venous disturbances (Kundrat,[5] Heschl,[9] Ghizzetti,[10] Jaffé,[11] Holtby,[12] Alpers and one of us [C. A. P] [13] and others); (*b*) inflammatory lesions, including undetermined infections, syphilis and tuberculosis (Virchow,[14] Strümpell,[15] Schultze,[16] von Limbeck,[17] Globus,[18] Winterode and Lewis,[19] Seelig-

9. Heschl, R.: Neue Falle von Porencephalie, Prag. Vrtljschr. f. d. prakt. Heilk. **100**:40, 1868.

10. Ghizzetti, C.: Contributo alla conoscenza della porencefalia (lue e lesioni venose), Pathologica **23**:575 (Oct. 15) 1931.

11. Jaffé, R.: Traumatic Porencephaly, Arch. Path. **8**:787 (Nov.) 1929.

12. Holtby, J. R. D.: A Study of Porencephaly with Special Reference to a Case of Symmetrical Lesion Affecting the Temporal Poles of the Cerebrum, Tr. Roy. Acad. M. Ireland **36**:207, 1920.

13. Patten, C. A., and Alpers, B. J.: Cerebral Birth Conditions, with Special Reference to the Factor of Hemorrhage, Am. J. Psychiat. **12**:751 (Jan.) 1933.

14. Virchow, R.: Congenitale Encephalitis und Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867.

15. Strümpell, A.: Ueber die acute Encephalitis der Kinder (Poliencephalitis acuta, cerebrale Kinderlähmung), Jahrb. f. Kinderh. **22**:173, 1884.

16. Schultze, F.: Beitrag zur Lehre von den angebornen Hirndefecten (Porencephalie), Heidelberg, C. Winter, 1886.

(Footnotes continued on next page)

müller [20] and many others), and (*c*) traumatic factors (Schröer [21] and Jaffé [11]).

3. *Symptomatology.*—In the literature clinical studies in cases of porencephaly are rather infrequent as compared with the large amount of pathologic material. A detailed consideration, therefore, of the various clinical findings, even in this small group, seems advisable.

A. Mental Status: Three of the patients in our series (cases 4, 6 and 9) were mentally retarded, and one (case 6) was also delinquent. A search of the literature failed to reveal any statistical data regarding the mentality of patients with porencephaly.

B. Evidences of Abnormalities Which Had Existed Since Early Childhood: These were of considerable interest, as their presence, in our opinion, suggests the existence of porencephaly. The most striking of these findings was a definite lack of development in one half of the body, which was present in seven of the nine patients (cases 1, 2, 3, 4, 5, 6 and 9). This lack of development contrasts sharply with normal development in case 8, in which porencephaly developed at the age of 17 years, after trauma. In one patient (case 7) there was no lack of development, except equinovarus on the side involved. Equinovarus was also present in case 4. Hydrocephalus was present in only one instance (case 4). It is of further interest that the patients were left handed, which was accounted for later by the presence of most of the cysts on the left side of the brain.

C. Convulsive Phenomena: This symptom was present in all cases and was the cause of the patient's coming to the clinic. All the nine patients had jacksonian fits. In addition, four (cases 2, 6, 7 and 8) had generalized convulsions. The time of onset of the convulsions varied: in one patient at birth, in one at the age of 3 years, in one at the age of 4, in one at the age of 10, in two at the age of 11, in one at the age of 12, in one at the age of 14 and in one at the age of 17 years. The last patient began to have convulsions at the time of occurrence of the trauma. It is of interest that in case 3 the onset of convulsions coincided with commencement of the menses. None of the patients had petit mal attacks. We are unable to state in what percentage of all recorded cases of porencephaly convulsions were present.

D. Other Motor Disturbances: In all cases in which inception of convulsions was in early life evidences of motor weakness or disturbance of unilateral reflexes were shown. In five instances (cases 2, 3, 4, 6, and 9) definite hemiparesis was revealed. In case 7 only a central facial palsy was shown, in case 5 weakness of the lower part of

17. von Limbeck, R.: Zur Kenntnis der Encephalitis congenita und ihrer Beziehung zur Porencephalie, Ztschr. f. Heilk. **7**:87, 1886.

18. Globus, J. H.: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

19. Winterode, R., and Lewis, N. D. C.: A Case of Porencephalic Defect Associated with Tuberculous Encephalitis, Arch. Neurol. & Psychiat. **10**:304 (Sept.) 1923.

20. Seeligmüller, A.: Ueber Lähmungen im Kindesalter, Jahrb. f. Kinderh. **13**:226 and 315, 1879.

21. Schröer: Zur Kenntnis der traumatischen Porencephalie, Virchows Arch. f. path. Anat. **262**:144, 1926.

the face and the arm and in case 1 weakness of the hand only. It is to be observed, therefore, that, in addition to lack of development and convulsive phenomena, motor weakness accompanied by changes in tone and reflexes was found in all cases in this series.

E. Sensory Disturbances: Hemianesthesia was present in three instances (cases 2, 7 and 9) and hemianopia in four (cases 2, 3, 7 and 9). Each of the patients with hemianopia was unaware of its existence, indicating that a defect unknown to the patient had been present for a long time. Atrophy of the optic nerve of varying degree was found in cases 4, 5 and 7.

These sensory findings are of considerable significance from an etiologic standpoint. In Little's disease and allied conditions, in which there is paralysis from early life, the motor system only is involved, a finding that was discussed at length by one of us (C. A. P.)[22] Apparently, whatever the etiology of porencephaly, it differs in its clinical manifestations from that of the aforementioned conditions by reason of these sensory findings. Of further interest is the report of a case by Jelsma, Spurling and Freeman[23] in which the absence of the occipital lobe of the brain due to porencephaly was associated with essentially normal vision.

F. Roentgenographic Findings: In all cases the diagnosis of porencephaly was confirmed by roentgenographic findings. The criteria for the roentgenologic diagnosis of porencephaly were stated by Dr. Karl Kornblum as follows:

> The roentgenologic diagnosis of porencephaly is dependent on air studies, either encephalography or ventriculography. The condition, however, may frequently be suspected from ordinary roentgen examination of the head. In cases in which there is asymmetry of the skull, one side being smaller than the other, a porencephalic cyst is often found in the smaller hemisphere. Such asymmetry denotes hemiatrophy of the brain, in consequence of which the affected side of the skull is also atrophic. In addition to being smaller, the cranium on the affected side presents thickening of the bones of the vault; the petrous pyramid, mastoid and frontal ethmoid sinuses on the same side show a greater degree of pneumatization. Roentgenographic appearance of this kind should lead one to suspect the presence of a porencephalic cyst in the atrophic hemisphere. Porencephaly may also be found in association with the hydrocephalic skull.
>
> In the air studies porencephaly generally presents itself as a single cavity, usually unilateral, of variable size and most commonly located in the parietal or occipital region, although the cyst may occur anywhere. Cavities of this type may be multiple and bilateral. The vast majority that are shown in the roentgenogram are in communication with one of the lateral ventricles. Porencephaly is a manifestation of cerebral atrophy; therefore, in addition to the air-filled cavity, there are other evidences of atrophy of the brain. The condition is revealed by the marked enlargement of the subarachnoid pathways. This may be bilateral, although

22. Patten, C. A.: Cerebral Birth Conditions with Special Reference to Cerebral Diplegia: A Preliminary Report of a Clinical Study, Arch. Neurol. & Psychiat. **25**:453 (March) 1931.

23. Jelsma, F.; Spurling, R. G., and Freeman, E.: Absence of Occipital Lobe of Brain (Porencephaly) with Essentially Normal Vision, Arch. Neurol. & Psychiat. **28**:160 (July) 1932.

not infrequently on the same side as the porencephaly the pathways are obliterated, owing to arachnoiditis. The cerebral hemisphere containing the cyst is frequently smaller, in consequence of which there is lateral displacement of the ventricular system toward the cystic side. As a manifestation of atrophy of the brain, the basal cisterns are increased in size, and there is a variable amount of subdural air beneath the tentorium. Cerebellar atrophy may be shown by exaggerated visualization of the cerebellar gyri. Ventricular dilatation is dependent on the degree and distribution of atrophy of the brain. When this is marked and generalized, there may be enormous internal hydrocephalus. Porencephaly in such cases plays a minor rôle. Porencephaly resulting from localized trauma may be the only abnormality revealed in the air films, although usually there is localized arachnoiditis over the cyst and the portion of the lateral ventricle adjacent to the porencephalic cyst is slightly dilated and drawn toward the cavity.

In the roentgen examination one must not mistake a dilated portion of the lateral ventricle for a porencephalic cyst. This differentiation is not always easy. The lesion which may simulate porencephaly is a gliomatous cyst. In this condition the evidence of atrophy of the brain is usually lacking; the ventricles are more frequently encroached on than dilated, and the ventricular displacement is toward the side opposite the cyst.

G. Location of the Porencephalic Cyst: It is of interest that in eight of the nine cases the cyst was in the left cerebral hemisphere. In three cases it was largely in the parietal region, in one in the fronto-parietal, in two in the parieto-occipital, in one in the temporoparietal, and in two in the frontal.

In Siegmund's [7] report of one hundred and twenty-two cases of porencephaly the region of the central fissure was most frequently affected. The frontal lobe was involved in seventeen cases, the temporal in thirteen, the occipital in fourteen and the basal ganglia in twenty-four. Holtby [12] in 1918 reported a case of bilateral porencephaly in a woman aged 73.

4. *Surgical Pathologic Observations and Operative Procedures.*—When the surgeon exposes a porencephalic cyst at the operating table, two questions demand an answer. First, how can such marked destruction of large areas of the brain be accompanied by relatively mild neurologic symptoms? Second, how can surgical measures in any way benefit a patient with such a lesion? Foerster and Penfield,[24] Penfield [25] and others suggested that a cause of focal epilepsy is a scar in the brain tugging on and irritating active cortical areas. They implied that bands of heavy glial tissue form about the site of an injury and swing inward from the cortex toward the ventricle and that, as the fluid in this area pulsates with each heart beat, the impulse is transmitted along the scar to the cortex. This constantly repeated mild stimulation of excitable centers results in a focal convulsion.

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24. Foerster, O., and Penfield, Wilder: Der Narbenzug am und im Gehirn bei traumatischer Epilepsie in seiner Bedeutung für das Zustandekommen der Anfälle und für die therapeutische Bekämpfung derselben, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:475, 1930; Brain **53**:99, 1930.

25. Penfield, Wilder: The Radical Treatment of Traumatic Epilepsy and Its Rationale, Canad. M. A. J. **23**:189, 1930.

In a case of porencephalic cyst the situation is somewhat different. The enlarged ventricle has already extended to within a millimeter or two of the surface, being covered only by a thin shell of degenerated cortex, held in place apparently by the overlying vessels, the pia and the arachnoid. No functioning cells can be present in this tissue. If tugging on active centers is the cause of focal epilepsy accompanying such a cyst, the pull must be lateral, on adjacent areas.

In the first case in this series the revealed pathologic condition was a surprise. The whole left frontal lobe up to the anterior edge of the prefrontal convolution, as far down as the sylvian fissure and upward to the falx, had been replaced by a cyst. Over this cyst was a thin, smooth, velvety membrane containing many vessels, large and small, covered by the arachnoid. Slight remnants of the architecture of the sulci and gyri could be made out from the course of these superficial vessels. Since no other procedure was known, this membrane was removed up to the edge of the apparently normal brain. The anterior third of the left ventricle was then visible, with the choroid plexus of the left ventricle, the foramen of Monro, the septum pellucidum and the choroid plexus from the right ventricle all exposed. With the idea of checking the secretion of cerebrospinal fluid from the choroid plexus and thereby preventing immediate refilling of the cyst, the choroid plexus of the left ventricle was removed, and the vessels supplying that of the right ventricle were clipped.

The boy was carefully watched, and when, six months later, a somewhat similar condition of porencephaly appeared, we believed that the procedure had justified itself and could be repeated with safety. Excision of the roof of the cyst and interference with the function of the adjacent choroid plexus were the surgical attack on each occasion. That coagulation and removal of the choroid plexus may be carried too far is illustrated in case 7. The plexus was coagulated up to the foramen of Monro but was not removed. Subsequently, scar tissue formed, obliterating the foramen on this side and producing increasingly large unilateral hydrocephalus. Four operative attempts to create a new foramen or to by-pass the fluid through an artificial opening into the third ventricle failed. The last operation resulted in fatality. The other fatality (case 8) resulted from poor surgical judgment. A cranioplasty to cover a frontal cranial defect had been successfully performed, resulting in considerable diminution of the number and severity of the fits. On the patient's second admission to the hospital, we attempted to remove scar tissue from both frontal lobes to a dangerously wide extent, instead of operating on each side separately.

From the surgical standpoint, the impressive fact in this series of cases has been that a surgical procedure which seemed to increase the damage and was adopted simply through lack of a better approach has been of benefit. It is true that none of the patients has been observed over four years. Eventually it is conceivable that convulsions may recur. During the relatively short period of observation, however, and in a small series of cases, the results have been satisfactory and commensurate with the operative risk.

5. *End-Results.*—Of the eight patients on whom operation was performed, two died. Of the six surviving patients three have had complete relief from convulsions, while the other three have shown marked improvement. One patient showed great improvement in the hemiplegia.

COMMENT

This study brings out certain facts which are useful for diagnostic and therapeutic purposes and at the same time raises questions the answers to which, when revealed in the future, may prove of value in the management of epilepsy.

The evidence deduced from the study tends to show that in the majority of cases a porencephalic cyst has its inception early in life. At least this applies to the group of patients who seek aid because of convulsive seizures. Except for the time of development, this study does not present data concerning the etiology. The etiology and pathogenesis are obviously different from those of the cerebral diplegias of childhood. In cases of the latter condition the symptoms are bilateral and exclusively motor, while in cases of porencephaly they are localized and frequently associated with sensory disturbances. It cannot be stated with certainty whether the involvement of branches of one of the three major arteries of the brain explains this localized lesion.

We have no explanation for the occurrence of the lesion on the left side in eight of the nine cases. Nor have we a satisfactory explanation for the disproportion between the great loss of brain substance and the mild degree of functional disturbance. It appears likely that the destruction of the brain and its replacement by fluid must have been a slow process, thus enabling adjacent centers to take over the functions of the ablated areas. This again suggests development of the lesion in early life.

We have no satisfactory explanation for the occurrence of convulsions in these cases. Certainly, there was no formation of scar tissue to tug on overlying cortical centers. The cortex covering the cyst was so thin and atrophic that it must have been functionless. If the irritation producing focal epilepsy was caused by traction on adjacent areas, the removal of the thin wall of the cyst could hardly have altered conditions sufficiently to reduce this stimulation. In some cases the thin layer of cortex lying over the cyst was highly vascularized. A vasomotor reflex might conceivably have affected neighboring sensitive centers and produced a fit.[26] In other cases the outer wall of the cyst was practically avascular. In most cases the choroid plexus in the underlying ventricle was clipped, in one instance in both lateral ventricles. But it is hardly probable that the slight interference with cerebrospinal fluid filtration could account for the cessation of convulsions.

To compensate for these unanswered questions, we offer certain criteria which, in our opinion, may be used for establishing a clinical diagnosis of porencephaly and may lead to encephalographic studies and relief by surgical procedures. Failure of development of one half, or

26. Forbes, H. S., and Wolff, H. G.: The Cerebral Circulation: III. Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928. Wolff, H. G., and Forbes, H. S.: The Cerebral Circulation: IV. The Action of Hypertonic Solutions: Part I, ibid. **20**:73 (July) 1928. Kubie, L. S., and Hetler, D. M.: The Cerebral Circulation: IV. The Action of Hypertonic Solutions: Part II. A Study of the Circulation in the Cortex by Means of Color Photography, ibid. **20**:749 (Oct.) 1928. Wolff, H. G., and Forbes, H. S.: The Cerebral Circulation: V. Observations of the Pial Circulation During Change in Intracranial Pressure, ibid. **20**:1035 (Nov.) 1928.

part of one half, of the body, accompanied by weakness of the upper motor neuron type, sensory disturbances and jacksonian fits, justify the diagnosis of a lesion which had its inception in early life and is probably a porencephalic cyst. The diagnosis in the majority of cases in this series was established before encephalographic studies were made. The air studies made the diagnosis definite. Considering the end-results in these cases, surgical intervention seems to be indicated.

REPORT OF CASES

CASE 1.—*A boy aged 13, born in difficult labor, who did not begin to talk until the age of 3 years and 6 months, first had jacksonian convulsions on the right side when 11 years of age. Examination revealed lack of development and weakness of the right arm. An encephalogram disclosed a porencephalic cyst in the left frontal region, and operation resulted in marked reduction in convulsions.*

History.—J. H., a Negro boy, was admitted to the Hospital of the University of Pennsylvania on July 31, 1931. There was a history of difficult and prolonged delivery, without instruments. Development was normal, except that the boy did not talk until 3 years and 6 months of age. He still hesitates in his speech, stutters and at times cannot find or say the word he wants. In 1929, two years before his admission to the hospital, at the age of 11, he commenced to have convulsions on the right side. These began with twitching of the fingers of the right hand and flexion of the fingers and arm and then involvement of the right leg and jerking of the whole body. After the convulsions began, the speech defect became much more pronounced. The duration of the convulsions varied from ten to thirty minutes, and the patient had as many as four in one day, although they usually occurred about once a month.

General Physical Examination.—The results were normal.

Neurologic Examination.—The boy was cooperative and of about average mentality for his age. The left hand grip was more powerful than the right, and for this reason he tended to be left handed. The reflexes were normally active, and no pathologic reflexes were present. The optic fundi, visual fields and acuity were normal.

Laboratory Data.—Studies of the blood, urine and spinal fluid, including serologic tests, gave normal results. The spinal fluid pressure with the patient in the erect position was 500 mm. of water.

Roentgen Examination (Dr. H. Pancoast).—Encephalographic studies showed a large porencephalic cyst in the left frontal region, apparently incompletely drained (fig. 1).

Operation.—On August 11 one of us (F. C. G.) reflected a left frontotemporal bone flap. Opening the dura disclosed a remarkable picture. The left cerebral hemisphere to the precentral convolution was replaced entirely by a cyst. Over this cyst there was a thickened membrane, presumably the preexisting arachnoid. This membrane was rather vascular, with blood vessels running into it from the cortex. The membrane was excised, the vessels being carefully clipped, and through the cyst one could look directly into the left lateral ventricle. The choroid plexus was seen plainly. The septum pellucidum lay at the bottom of the wound, and through the rather enlarged foramen of Monro one could see into the right ventricle as well.

A portion of the septum pellucidum was excised, exposing the choroid plexus of the right ventricle and the large vessel running into each choroid plexus. These

were clipped, in the hope that it might interfere to some extent with the output of cerebrospinal fluid. The bone flap was replaced and sutured, without drainage. Recovery followed a rather stormy postoperative period.

Course.—Since operation the boy has been seen repeatedly. On Jan. 4, 1933, it was noted that his mentality had improved; speech was excellent, and he had had no convulsions. On Oct. 17, 1934, he reported that he had had no convulsions, but speech was slightly hesitant; he had been working and wanted to learn to drive a car. On Sept. 18, 1935, he reported that a week before he had had an attack of dizziness, without falling or loss of consciousness. This was the only attack which in any way suggested the former spells. The attack lasted only a few minutes. Aside from poor memory and slight hesitation in speech, he appeared normal. He was seen again in December 1936. He had had no more dizzy spells and was working.

CASE 2.—*In a girl who had previously been normal there developed at the age of 3 years, after an injury to the roof of the mouth, right spastic hemiplegia with*

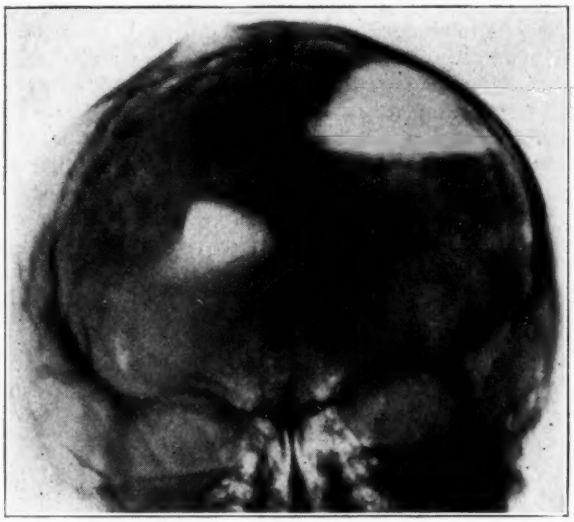

Fig. 1.—Encephalographic study in case 1, showing a porencephalic cyst in the left frontal region.

jacksonian convulsions on the right side. Examination revealed right hemiplegia and marked lack of development of the right extremities. The diagnosis of porencephaly was confirmed by encephalography, and operation was followed by cessation of attacks and marked improvement in muscular power.

History.—M. H., a girl aged 16 years, was admitted to the Graduate Hospital of the University of Pennsylvania on Jan. 27, 1932, complaining of paralysis of the right arm and convulsions. The family and past medical histories were without significance. At the age of 3 years the patient accidentally ran a piece of wood into the roof of her mouth, but with no great force, as it did not cause hemorrhage or abrasion. That night she had a convulsion, which started with twitching at the mouth, followed by twitching of the right arm and leg. The next day she had paralysis of the right arm and weakness of the right leg. She could neither walk nor talk for six months but showed slight improvement in the paralysis. There were no further convulsions until the age of 11, since which time they had become

progressively more severe and frequent. The convulsions occurred at any time, day or night, beginning with twitching of the fingers of the right hand, then involving the arm and the leg and finally becoming generalized. They were always accompanied by loss of consciousness and occasionally by biting of the tongue, but not by incontinence. After each convulsion there was transient increase of paralysis of the right arm. The convulsions were more frequent and severe just before and after the menstrual period.

Physical Examination.—The patient was fairly well developed and nourished and of average mentality. She presented no evidence of any definite somatic disturbance.

Neurologic Examination.—Examination of the sense of smell and ophthalmologic studies showed no deviations from the normal. The left pupil was slightly larger than the right; both were regular and responded well to light and in accom-

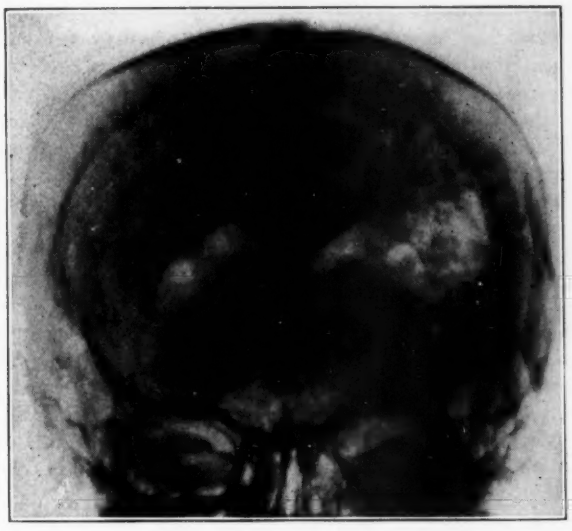

Fig. 2.—An anteroposterior encephalogram taken in case 2, showing a porencephalic cyst in the right temporoparietal region.

modation. There were slight nystagmoid movements on extreme rotation of the eyes; otherwise, all extra-ocular movements were normal. Neither sensory nor motor components of the fifth nerve were involved. There was slight weakness of the right lower part of the face. Hearing was unimpaired, and the Bárány test revealed no definite abnormality in the vestibular pathways. All other cranial nerves were essentially normal. There was definite spastic paralysis of the right arm and leg, more marked in the arm. The reflexes were more exaggerated on the right, and there were Babinski and Hoffmann signs on the right. The abdominal reflexes were active bilaterally. The right arm and leg were definitely smaller than the left, but the musculature was firm. There were no definite sensory disturbances, although the perception of pain and touch was perhaps a trifle less distinct on the right than on the left. Synergic control was normal on the left side and unsatisfactory on the right, owing to the spastic paralysis. Speech was a trifle slurring, and test phrases were pronounced with difficulty.

Laboratory Findings.—Urinalysis, a blood count and blood chemistry studies revealed no abnormalities. The Wassermann reaction of the blood was negative; examination of the spinal fluid gave normal results in every respect, including pressure.

Roentgen Examination (Dr. G. E. Pfahler).—Roentgenograms of the skull revealed no abnormalities. An encephalogram revealed an irregularly defined area of porencephaly in the upper portions of the left precentral convolutions, measuring approximately 4 cm. in diameter. There was deviation of both ventricles to the left, with retraction of the left lateral ventricle upward and outward (fig. 2).

Operation.—On Feb. 18, 1932, with the patient under anesthesia induced with tribromethanol in amylene hydrate and procaine hydrochloride, one of us (F. C. G.) reflected a left frontotemporal bone flap. The dura was not tense and was opened widely. In the upper part of the flap there appeared a large subcortical cyst, which extended nearer the midline than had been suspected. The bone flap was therefore enlarged to the midline by removing an extra half-inch (1.27 cm.) of bone in a solid piece. This bone was saved and eventually wired to the bone flap.

The cyst was then attacked, the cortical vessels running into it being clipped and the entire roof of the cyst removed, together with the thin vascular cortex forming the edge of the cyst. This was accomplished without great difficulty, although the part of the cortex involving the roof of the cyst was quite vascular. The central part of the cyst had a number of long, shreddy blood vessels running over the surface and into the depths. At the bottom of the cyst there was an area of scar and degenerated brain tissue, about 2 by 2 by 2.5 cm., which was excised. After hemostasis accompanying this step of the operation was completed, the lateral ventricle was sought but was not seen. The dura was then closed over the cyst cavity and sutured. Decompression was effected by removing about one half of the base of the flap, without opening the dura. A drain was passed into the cyst cavity and carried out through a stab wound behind the edge of the incision. The piece of bone which had been removed was wired to the bone flap, and the bone flap was wired to the bone edge of the incision in two places. Hemostasis having been carefully completed, the wound was closed in layers. The patient's condition was satisfactory at all times.

Course.—At the last contact, in January 1936, the patient stated that she had had no more convulsions and that the power in the right extremities had markedly improved. She no longer limps and can dance. Power in the right hand has returned almost to normal.

CASE 3.—*A girl who after normal birth had cyanosis for the first week of life and a convulsion at the end of the first year began to have jacksonian convulsions on the right side at the age of 11 years. Examination revealed slight right hemiparesis and right hemianopia. The diagnosis of a porencephalic cyst was confirmed by an encephalogram; after operation the convulsions ceased.*

History.—R. L., a girl aged 15 years, was admitted to the Graduate Hospital on June 19, 1935. The patient was born at full term, with normal delivery, and weighed 7½ pounds (3,402 Gm.). She was cyanotic during the first week of life. She began to walk at the age of 19 months and to talk at 2 years. She had a generalized convulsion at the age of 1 year. At the age of 11 years, coincident with the onset of menstruation, she began to have jacksonian convulsions on the right side, which were initiated by a cramped feeling in the right hand and fingers, followed by stiffness in the right arm and leg, falling to the floor and usually biting of the tongue. The convulsions lasted a minute or two; after recovery she felt nervous and shaky but not drowsy. The seizures occurred about every two months.

General Physical Examination.—The patient was thin and apprehensive but otherwise normal.

Neurologic Examination.—There was slight weakness of the right side of the face and of the movements of the right hand and arm. To a lesser extent the right leg was weak, with increase of tendon reflexes. There was right homonymous hemianopia, but the optic fundi were normal.

Laboratory Data.—Studies of the blood, urine and spinal fluid gave normal results.

Roentgen Examination (Dr. Robert Shoemaker III).—Flat films showed no particular abnormalities. An encephalogram revealed a large porencephalic cyst in the posterolateral portion of the left cerebral hemisphere, apparently due to enlargement of the posterior horn of the left lateral ventricle (fig. 3).

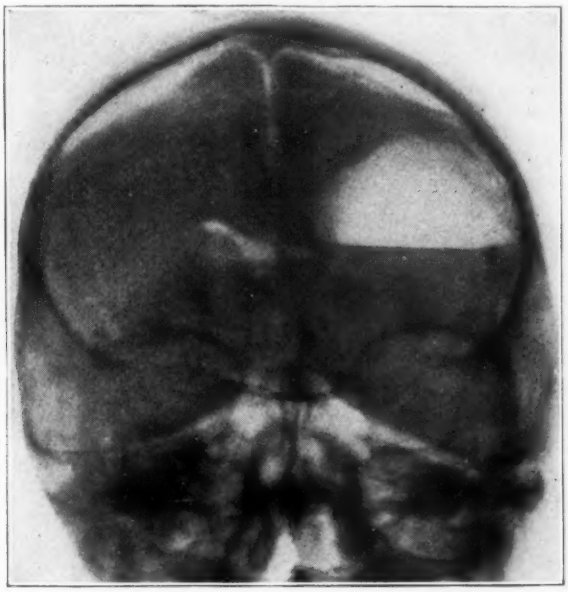

Fig. 3.—Encephalographic study in case 3, showing a porencephalic cyst on the left side.

Course.—After encephalography and the institution of a dietary regimen, together with the administration of phenobarbital, the patient had few attacks for one year. Then, in spite of treatment, the attacks became more frequent, and operation was advised.

Operation.—On June 20, 1935, one of us (F. C. G.) reflected a large parieto-occipital bone flap on the left side without difficulty. The dura was opened, and a remarkable picture presented itself (fig. 4). The whole left occipital lobe, from about the level of the supramarginal gyrus downward and posteriorly to the tip of the occipital lobe, was cystic. At the lower part of the cyst, just above the lateral sinus and for 2.5 cm. upward, nothing was left but the wall of the cyst. At about the level of the supramarginal gyrus, the wall shaded into an area in which curious thin islands of cortex remained in the cyst. The cyst extended upward to within

about 3 cm. of the midline and anteriorly to about the edge of the parietofrontal region, i. e., the posterior edge of the frontal and the anterior edge of the parietal lobe.

The vessels running from the roof of the cyst were ligated and removed with the Bovie knife. The cyst was then completely uncapped (fig. 5). The

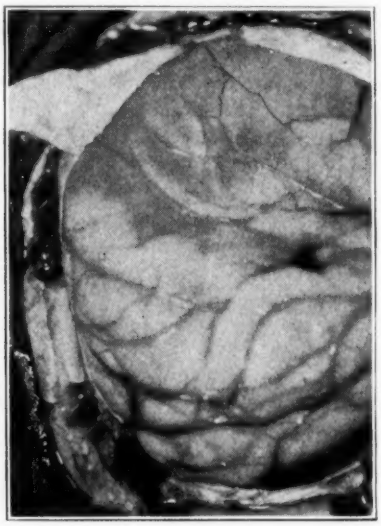

Fig. 4.—Photograph of the operative field, showing the appearance of the cyst in case 3.

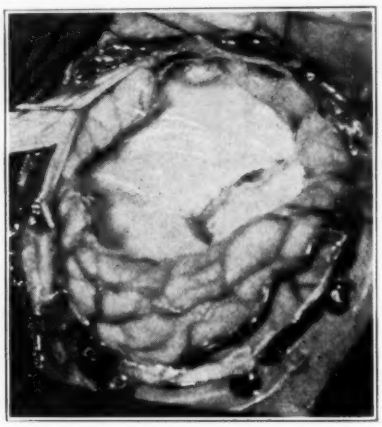

Fig. 5.—Photograph of the operative field after excision of the cyst in case 3, showing the ventricle and the choroid plexus lying in the floor of the ventricle.

choroid plexus could be seen running from the anterior horn of the left lateral ventricle into what had been the descending horn of the left lateral ventricle. The cyst seemed to spring from the ventricular vestibule. The opening was

enlarged; through it the choroid plexus protruded; this was picked up and coagulated, and its large vessels were removed, as well as the part which reaches into the descending horn of the lateral ventricle.

The dura was replaced and sutured and a decompression provided. The bone flap was replaced and wired, and the skin was closed in layers, without drainage (fig. 6).

Course.—The patient was seen on Jan. 2, 1937, eighteen months after the operation. She had had no spells of any kind; vision had improved, and she had gained in weight. She was back at school and was apparently normal.

CASE 4.—*A boy after a normal delivery showed signs of enlargement of the head at the age of 4 months, had diphtheria and convulsions in early childhood, did not walk or talk until 5 years of age and was mentally retarded. At the age of 14 there developed jacksonian convulsions on the right. Examination showed failure of development of the right side, atrophy of the optic nerve, enlargement of the head and right hemiparesis. The diagnosis of porencephaly was confirmed by encephalography, and operation produced marked improvement.*

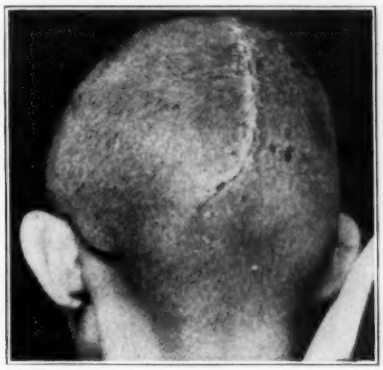

Fig. 6.—Photograph taken after operation in case 3, showing the position of the operative scar.

History.—S. B., a boy aged 14 years, was admitted to the Graduate Hospital on June 1, 1935, with the chief complaint of pain in the right arm and jacksonian convulsions on the right side. The family history was without significance, except that a sibling had convulsions in infancy but apparently recovered. The patient was the fourth of six children; he was born at full term, with normal delivery. He began to walk and talk at the age of 5 years. As a small child he had diphtheria and convulsions on two occasions. The father did not remember whether the convulsions were on one side or both; while the child appeared normal at birth, it was noted that at the age of 3 or 4 months the head was abnormally large. The patient entered school at the age of 7 and failed of promotion twice. The most difficult subjects were history, electricity and shop work. When about 5 years of age he caught his right arm in a wringer and was in the hospital for four weeks, undergoing reparative operations.

In the early part of October 1934 the patient's father observed that the child had attacks in which the right side of the face, right arm and right leg became weak. This lasted a few seconds, during which he was speechless. At first the spells occurred every two weeks, but in November 1934 they increased to a few

daily. In addition to the weakness, there was rigidity of the muscles, without visible movements. The boy complained of pain in the right arm, most marked in the hand but not involving the face or neck. In April 1935 he began to have frank convulsive seizures localized to the right side, beginning in the hand and spreading to the face, arm and leg. These spells were usually accompanied by loss of consciousness. At times the patient complained of numbness on the right side of the body preceding and following the spells. In addition, there was complaint of headache, but no visual disturbances, tinnitus or vomiting. In November 1934 he complained of abnormal odors, such as that of musty eggs. The child had shown progressive mental dulness since the fall of 1934. He slept well at night but did not fall asleep in the daytime. There was no history of excessive urination or undue or sudden increase in the size of the hands or feet.

Physical Examination.—Somatic examination gave normal results. The boy had a distinctly abnormal head, with expansion of the upper part.

Neurologic Examination.—Cranial Nerves: The sense of smell was defective bilaterally. There were no cuts in the visual fields. The disks of both eyes, but especially the right, were sharply demarcated, and the color was distinctly pale; the arteries were smaller than normal, as compared with the veins. The pupils were equal and regular and responded to light and in accommodation. Visual acuity in the right eye was 6/15 and in the left 6/15. The palpebral fissures were about equal. All extra-ocular movements were normal. The fifth nerve was normal in both motor and sensory components; there was no corneal anesthesia. There was definite weakness of the right lower part of the face both on voluntary and on emotional movement. All other cranial nerves were normal.

Trunk: The abdominal reflexes were well preserved. The patient walked without swinging the right arm and favored the right side. There was no Romberg phenomenon.

Upper Extremities: The right upper extremity was distinctly smaller and weaker than the left, the difference being most marked in the hand. There were no changes in tonus, atrophy or tremors, but there was definite lack of development. The biceps and triceps reflexes were increased on the right, as compared with those on the left, but there was no Hoffmann sign on either side. Sensation, both deep and superficial, and stereognosis were normal on both sides. In the finger to nose test there was definite dysmetria on the right side.

Lower Extremities: The right leg was not as well developed as the left. There were no definite weakness except in walking and no change in tone, atrophy or tremors. The right foot differed distinctly from the left in that the arch was much deeper. The knee and ankle reflexes were more pronounced on the right than on the left; there was no clonus or Babinski sign on either side. All modalities of sensation were preserved bilaterally. The heel to knee test on the right side was carried out poorly.

Laboratory Data.—Urinalysis, a complete blood count, blood chemistry studies and Wassermann tests of the blood gave normal results. Spinal fluid studies revealed a slight increase in pressure but otherwise nothing abnormal.

Roentgen Examination: (Dr. Karl Kornblum).—The pituitary fossa was normal in appearance and measured 10 mm. in the anteroposterior diameter and 8 mm. in depth. There was unusual development of all the cranial sinuses, including the mastoids. There was definite enlargement of the head but no evidence

of increase in intracranial pressure to account for the enlargement. The left side of the head was slightly larger than the right. The bones of the vault on this side were thinner than those on the opposite side. While the paranasal sinuses were unusually large, they showed no asymmetry. The left mastoid and petrous pyramid were larger than the right. These findings are not those usually seen in association with hemiatrophy of the brain, which is a common cause of asymmetry of the head. It was evident from the large size of the head that the patient had hydrocephalus. The increase in the size of the left side seemed to indicate greater degree of hydrocephalus on this side. One might even suspect the presence of a porencephalic cyst on the left.

Encephalography: Sagittal views showed marked dilatation of the lateral ventricles. The left ventricle was somewhat larger and more irregular than the right. There was no lateral displacement. Little air was to be seen in the subarachnoid pathways. A large accumulation of air in communication with the left lateral ventricle was located along the midline near the vertex in sagittal views. This was a large porencephalic cyst. There was also dilatation of the third ventricle. Lateral views confirmed the evidence in the sagittal projections. The cyst was located in the left midparietal region. Some subarachnoid pathways in the region of the cyst were moderately dilated. The aqueduct and fourth ventricle showed considerable dilatation. There was an abnormal amount of air in the cisterna magna. Conclusion: There was a marked degree of generalized atrophy of the brain, with secondary hydrocephalus and a porencephalic cyst in the left midparietal region.

Operation.—On June 24, 1935, one of use (F. C. G.) reflected a large parietotemporal bone flap. The dura was tense. Exactly in the middle of the top of the dural incision was a thinned area of cortex, circular and measuring about 3 cm. in diameter. The dura was slightly adherent to the lower part and definitely adherent to the upper part of this area. After careful dissection, the dura was freed, except at the top close to the midline. It should be stated that the cap of the cyst was made up of cortex, white and avascular and from about 2 to 3 mm. in thickness. When this area had been removed, there could be seen the outward prolongation of the vessels of the left ventricle (fig. 7). One could also see into the third ventricle and across into the right lateral ventricle. There was, therefore, not only porencephaly but definite hydrocephalus, confirming the encephalographic findings.

The bulk of the choroid plexus was removed from the left ventricle; on looking into the right ventricle the main vessel supplying the choroid plexus on that side could be seen, and a clip was placed on it. These maneuvers were carried out with practically no bleeding. The dura was then replaced, tightly sutured and pulled up to the bone at all points. It had been pulled off the bone for quite a distance as the brain collapsed on the evacuation of fluid. After the dura had been replaced, the ventricles were filled with physiologic solution of sodium chloride to extend the brain.

Course.—When seen on Dec. 6, 1935, the patient appeared much brighter and more alert than before the operation. While before operation he had several attacks daily, at the time of examination he never had more than one. The spells were only momentary. The neurologic status had improved in that the right extremities seemed to him and to the examiner not as weak as formerly, and he had better use of the right hand.

CASE 5.—*A girl after a birth injury had jacksonian convulsions on the right side from birth to the age of 9 years and again from the age of 12 to the time*

of observation. Examination revealed lack of development of the right arm, weakness of the right side of the face and right arm and atrophy of the optic nerves. Encephalography showed left cerebral hemiatrophy, and operation confirmed the clinical diagnosis of a porencephalic cyst and relieved the patient of convulsions.

History.—M. T., a girl aged 18 years, was admitted to the Graduate Hospital on April 25, 1935, with the chief complaint of convulsions. The family history was without significance for neurologic conditions. The past medical history was likewise unimportant except for two operations on the eye, the nature of which is unknown, a year prior to the time of examination and the absence of vision in the left eye since birth. The patient dated the beginning of convulsions to birth because of the history of a birth injury. Up to the age of 9 years, she had convulsions, usually at night, lasting from two and one-half to five hours and occurring every three months. The entire right side of the body, including the face, was involved. An aura of numbness on the right side was the only warning that an attack was imminent. From the age of 9 to 12

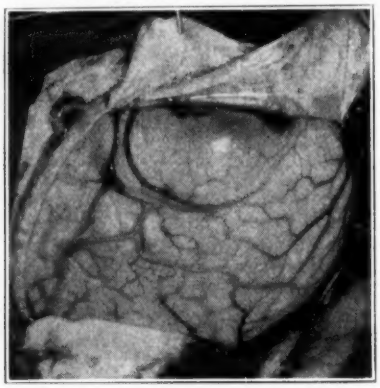

Fig. 7.—Photograph taken at operation in case 4, showing the cyst uncovered.

years she was free from attacks. From that time she had convulsions on the right side approximately every two weeks, which lasted about twenty minutes. Recently the convulsions had occurred about once a week. During the past month she had had severe headaches about once a week.

General Physical Examination.—The results were normal, except for large, pendulous breasts, coarse skin, a fine hairy growth over the limbs and marked perspiration of the hands and, to a less extent, of the feet.

Neurologic Examination.—The patient was well built. She was rather silly and facetious but of average intelligence. There was no definite facial weakness but some smoothness of the left side of the face in repose. Hearing was intact. There was no weakness of the palate or tongue. The right hand was smaller than the left, and the right hand grip was somewhat weaker. There was weakness of the movements of the right arm as compared with those of the left; it was not pronounced, however, and power was still good in this limb. There was no weakness of the lower extremities or ataxia. Sensation was intact throughout. All the tendon reflexes were normally active, and no abnormal reflexes were present.

Ophthalmologic Examination (Dr. L. C. Peter).—On April 26, 1935, visual acuity in the right eye was 6/15 with glasses and 6/22 without glasses; the left eye saw nothing. In repose there was left monolateral convergent strabismus; the eyes also were slightly rolled up; there was limitation of external rotation to the left in the left eye. When looking to the left nystagmus developed, with the quick component to the left; when looking to the right undulating nystagmus was present; on central fixation this changed to jerking nystagmus, with the quick component to the right. We believe this to be true ocular nystagmus. There was no true limitation of motion of the right eye, ptosis or exophthalmos.

The cornea and iris on the left were dull, with slight enophthalmos on that side; the pupil was large and did not respond to direct stimulation but responded consensually to stimulation of the right pupil. On the right the pupil was large, round and central and responded normally to all stimuli. Right Eye: The media were clear; the disk was oval and pale; the margins were distinct, and the cup, the ratio of the blood vessels and the macula were normal. The nerve head showed partial primary atrophy; this accounted for the fixation astigmatism. Left Eye: This eye was blind and showed an old retinal detachment, complete except for the superior temporal quadrant; the part of the retina which could be seen showed retinitis with marked degeneration. The condition was probably intra-uterine uveitis and was hopeless.

The patient showed complete right homonymous hemianopia.

Roentgen Examination (Dr. Karl Kornblum).—Examination of the head showed definite evidence of increased intracranial pressure, as denoted by diffuse convolutional atrophy. There was asymmetry of the head, the right side being larger than the left. The paranasal sinuses were unusually large, and there was extensive pneumatization of both mastoids, with evidence of pneumatization of the petrous pyramids. The appearance was that of cranial stenosis, with hemiatrophy of the left side of the brain.

The optic foramina were normal. The view of the base of the skull showed extensive pneumatization of the petrous pyramids. Pneumatization from the mastoids appeared to involve the adjacent portions of the sphenoid bone. We noted asymmetry of the sphenoid and maxillary sinuses, those on the left side being larger than those on the right. This conformed with the diagnosis of left hemiatrophy.

The encephalogram specifically demonstrated hemiatrophy of the left side of the brain. The ventricular system occupied a position to the left of the midline and there was a moderate degree of ventricular dilatation, the left lateral ventricle being considerably larger than the right. There was complete absence of air in the subarachnoid spaces on the left, except for a small accumulation in the posterior parietal region. The spaces on the right had not been completely drained. The pathways which were visible were normal in appearance. Overdevelopment of the nasal sinuses and the mastoid process on the left side were again well shown in this examination. Conclusion: The condition was hemiatrophy of the left side of the brain due to birth injury.

Operation.—On May 11 one of us (F. C. G.) reflected a left temporoparietal bone flap with a little difficulty, for the bone was vascular. The dura was not tense, but the middle meningeal artery was tortuous. There were many bleeding points over the surface of the dura, particularly at its upper edge along the longitudinal sinus. The dura was finally opened and the middle meningeal artery secured. There was also a bad bleeding point in the lower posterior angle of the wound, where the lateral sinus may have been involved.

When the dura was opened a large diffusely scarred area seemingly involved the posterior two thirds of the temporal lobe and extended backward into the occipital lobe. This scarred area seemed to involve particularly the part of the brain lying along the posterior two thirds of the sylvian fissure. In an attempt to see how far beneath the temporal lobe the scarred area extended, a number of small veins were observed running from the cortex to the neighborhood of the lateral sinus. Most of these were successfully coagulated, but when the largest had been seized in the forceps and was about to be coagulated, the patient suddenly moved her head, and the vein was torn off flush with the sinus. There was difficulty in controlling the bleeding. It was necessary finally to suture a piece of muscle over the rent in the sinus.

It was decided that the scarred area was too extensive to permit complete excision. The ventricle was therefore opened, and a hypertrophied choroid plexus, which was large and beefy, was exposed. This was carefully picked up, and as much as could be seen was thoroughly coagulated.

The dura was then cut about and resutured. It was pulled up to the bone at all points, and every effort was made to control completely all bleeding points. The flap was drilled for wiring, and about an inch of it was rongeured at the base for a decompression. The flap was replaced and wired, and the galea and skin were closed as usual in layers, with stab wound drainage behind the posterior limb of the flap.

Course.—When the patient was last seen she had had no convulsions but the curious creeping aura experienced prior to operation. There was no change in the neurologic picture.

CASE 6.—*A boy whose birth and early development were normal became completely paralyzed at the age of 3 years, after an acute illness; subsequently there developed generalized convulsions and left hemiparesis. Examination showed left hemiparesis, with athetoid movements of the left upper extremity and marked mental retardation. Encephalography and operation confirmed the diagnosis of porencephaly of the right frontoparietal region.*

History.—W. P., a white boy aged 18 years, was first admitted to the Graduate Hospital in October 1932. The family history was without significance. Birth and early development were normal; he walked at the age of 17 months and talked when 2½ years old. At the age of 3 years (in 1917) he was acutely ill; he became completely paralyzed and lost the ability to talk. After eighteen months he gradually began to walk and talk and at about the same time first had generalized convulsions. The convulsions were accompanied by loss of consciousness. He made poor progress in school and in the last three years became involved in petty thieveries. He was referred to the Graduate Hospital by the Juvenile Court. In addition, for several months prior to his admission he had had headache and vomiting spells.

General Somatic Examination.—The results were normal. The mentality was that of a low grade moron.

Neurologic Examination.—The fundi showed no abnormalities; there were no cuts in the visual fields, and visual acuity was normal. The pupils reacted sluggishly to light, and convergence was poor. There was definite left central facial palsy. All the other cranial nerves were normal. The left upper extremity was smaller than the right, but the muscles were firm, and there was no fibrillation. At rest the hand showed the customary position of hemiparesis, and the limb had a normal tone. Every few minutes the left forearm went into a tonic spasm and the

wrist into extreme ventral flexion, with hyperextension of the fingers except at the metacarpophalangeal joint. The bellies of the triceps and biceps muscles stood out prominently. The attacks could be induced by passive movement. The biceps and triceps reflexes were diminished on both sides. The left lower extremity was definitely underdeveloped and somewhat weak. All tendon reflexes were exaggerated, but more so on the left than on the right. There were no sensory or synergic disturbances. The gait was that of left spastic hemiplegia.

Laboratory Data.—Urinalysis and determination of the urea nitrogen and sugar contents of the blood gave normal results. There was mild secondary anemia. The Wassermann reaction of the blood was negative. The pressure of the spinal fluid was 10 mm. of mercury; globulin was increased, the Wassermann reaction was negative; the colloidal gold curve was 1221000000.

Roentgen Examination (Dr. George E. Pfahler).—No abnormalities were observed. An encephalogram taken on Oct. 26, 1932, was read as follows: In the lateral stereoscopic view the left lateral ventricle was completely visualized and showed slight uniform dilatation. The right lateral ventricle showed more dilatation, although this was not extreme. The posterior and inferior horns on the right side were not visualized. It is believed that this was due to failure to drain this area rather than to encroachment by a tumor, for, as seen in the anteroposterior and postero-anterior views, there was retraction on the right rather than displacement to the left, which one would expect if the disturbance were due to a tumor in this area. In addition, two rather sharply circumscribed areas were superimposed on the midportion of the bodies of the ventricles; the anterior area measured 13 mm. and the posterior about 22 mm. in diameter. These apparently represented cystic areas which communicated with the right ventricle. The third ventricle was slightly dilated. The aqueduct of Sylvius and the fourth ventricle were visualized. As seen in the anteroposterior and postero-anterior views, the right lateral ventricle was somewhat dilated and was retracted upward. The entire ventricular system showed a slight midline shift to the right. In the region lateral to the right ventricle there was an irregular decrease in density, which indicated that the diseased area was irregularly cystic. Conclusion: The condition was porencephaly, with a lesion involving the right side, in the right parietal and right frontoparietal regions. I cannot rule out involvement of the occipital lobe or of the basal ganglia.

Operation.—On Nov. 17, 1934, one of us (F. C. G.) reflected a moderately large temporoparietal bone flap, with the use of local anesthesia, revealing a normal-appearing dura, under no increased tension. About the middle of the operative site, corresponding to the position of the porencephalic cyst, there was a slight cone-shaped elevation of the bone, the dura and the cortex beneath. There were no adhesions. On turning back the dura the cortex appeared normal except for a marked increase in the number of arteries and veins along the sylvian fissure. About the middle of the operative field, in what appeared to be the sylvian fissure, there was a slight widening of the sulcus, with thinning of the arachnoid and several tortuous arteries and veins. This appeared to be at the exact site of the roentgenographic evidence of subarachnoid air and the porencephalic cyst.

The vessels were coagulated with the Bovie instrument, and an incision 1½ inches (3.8 cm.) long was made through this arachnoid area into the fissure. Rather tough white matter was encountered in passing through the cortex in the fissure. Within ½ inch (1.27 cm.) of the surface there was a bluish, thickened membrane, which proved to be the ependyma of the right lateral ventricle. This was incised, and clear cerebrospinal fluid gushed out. The opening into the lateral

ventricle was enlarged to about 1 inch (2.54 cm.) in diameter, revealing a normal-appearing right lateral ventricle as far as could be seen. The choroid plexus was abundant and was coagulated with the Bovie instrument from just behind the foramen of Monro to the point where the anterior horn curves into the temporal horn. At no time was any hemorrhage observed.

Palpation of the cortex along the sylvian fissure and around the edges of the transcortical incision revealed no further evidence of scar tissue. The induction coil was used on the cortex, but the patient was too deeply anesthetized to give any response. In view of the large number of vessels in the sylvian fissure and the lack of further evidence of scar tissue, no cortex was removed.

The dura, having first been cut close to the margin of the bony opening, was sutured in place after careful hemostasis. A few venous bleeding points along the outer border of the bony opening were stopped with muscle sutured to the periosteum. The bone flap was then replaced and sutured in position at numerous points by means of the periosteum. The skin was closed as usual in layers, without drainage.

Course.—The postoperative course was uneventful except that repeated tapping was required. When last heard from, the patient had had only three convulsions in nearly three years.

CASE 7.—*A boy whose mother had had influenza at two months of gestation suffered from convulsions for seven days after birth, a number of the major infections of childhood and a slight blow on the head some years prior to his admission to the hospital. At the age of 12 years jacksonian convulsions developed on the right side and later generalized convulsions. There was right hemiparesis, with equinovarus, hemihypesthesia and hemianopia on the right side. The diagnosis of a porencephalic cyst on the left side was confirmed by encephalography and operation.*

History.—B. R., a boy aged 14 years, was first admitted to the Graduate Hospital on Nov. 7, 1935. The family history was not of significance. The mother had had influenza when she had been pregnant two months. The boy had convulsions for seven days after birth and had had whooping cough, tonsillitis and diphtheria. Several years before his admission to the hospital he received a blow over the frontal region, which was unaccompanied by loss of consciousness. In 1931, at the age of 12 years, the patient began to complain of periods of stiffness of the right hand, especially the thumb and index finger. This occurred daily. The character of the convulsions then changed, beginning in the right hand, spreading to the right arm and then becoming generalized. There was loss of consciousness, but no biting of the tongue or lips, incontinence of urine or somnolence followed the attack. The patient was given phenobarbital but showed no improvement.

Examination.—The patient was intelligent and cooperative. General physical examination gave normal results. The neurologic abnormalities included slight pallor of the optic disks, right homonymous hemianopia, inability to wink the left eye, diminution of smell on the left side, left central facial palsy, increase of tendon reflexes on the right, absence of abdominal reflexes on the right, equinovarus of the right foot, hypalgesia of the right side of the body, including the face, and diminution in the sense of position in the right extremities.

Laboratory Data.—Laboratory studies made as a routine, including urinalysis, a blood count, blood chemistry determinations, Wassermann tests of the blood and examination of the spinal fluid, gave normal results.

Roentgen Examination (November 22, by Dr. Karl Kornblum).—There was asymmetry of the head as seen in the anteroposterior films. The left side of the

cranium was smaller than the right. In addition, the appearance of the left posterior parietal region suggested the possibility of an old depressed fracture. The pineal body showed a slight shift to the left. In the lateral view there was a small area of calcification just above the sella turcica; it was evidently due to slight calcification in the falx cerebri and from its position suggested that the falx was slightly displaced to the left. The pituitary fossa was normal in appearance and measured 9 mm. in the anteroposterior diameter and 7 mm. in depth. Conclusion: There was hemiatrophy of the left side of the brain, probably due to trauma at birth or during infancy.

Encephalography: In anteroposterior views the ventricles were of normal size and shape. The third ventricle was slightly dilated. The ventricular system was slightly drawn to the left. In the left parietal region there was a moderate-sized collection of air, which was globular and measured approximately 3 cm. in diameter. In lateral view this globular shadow was in the posterior parietal region. The aqueduct and fourth ventricle were of upper normal size. The basal cisterns were normal in appearance. The subarachnoid pathways were slightly exaggerated, particularly at the vertex of each hemisphere. Conclusion: There was porencephaly of the left posterior parietal region, with bilateral atrophy of the brain, more marked on the left.

First Operation.—On Feb. 3, 1934, with the patient under anesthesia induced with tribromethanol in amylene hydrate, ether and procaine hydrochloride, a temporoparietal bone flap was reflected. The exposure was bloody. The dura did not appear to be tense. At the top of the incision there were a number of large veins in the dura. The bone in this region was honeycombed with veins, and there was considerable bleeding from it and from the dura.

The dura was opened from below upward. In the postrolandic region and about the supramarginal gyrus was a pear-shaped area of scar tissue in which the cortex was flat, without the normal sulci and gyri, there was a larger amount of fluid in the subarachnoid spaces, the veins were more numerous and the color of the brain was pinker than elsewhere. The apex of this pear-shaped scar was directed anteriorly and inferiorly, extending about diagonally across the bone opening. Palpation of this area showed that it was cystic and that there was fluid beneath the scar tissue. Starting from below upward, the blood vessels running into this region were caught, and the area was excised to the ventricle. The lateral wall of the vestibule of the left lateral ventricle was removed, together with the scar, and then brain tissue lying above and lateral to the part of the ventricular horn that swings posteriorly to form the posterior part of the ventricle. The lower part of the excised area was over the inferior horn of the ventricle. After the excision no adjacent hard area suggesting scar tissue could be palpated. The area excised was roughly 6 cm. long and 3 cm. wide. The choroid plexus lay directly in view after the ventricle was exposed. It was larger and more plum-colored than usual. It was coagulated with the Bovie instrument. After complete hemostasis the dura was drawn back and sutured in place; the bone was wired and the scalp sutured in layers as usual, with stab wound drainage behind the posterior limb of the flap. The boy's condition on leaving the table was fair, but three or four hours after operation transfusion was necessary.

Course.—The patient was in the hospital on several occasions during a period of almost a year and underwent several operations. Several weeks after the first operation there developed an infection, which continued until it was necessary to remove the bone flap. Subsequently, the wound healed, but there was persistent bulging in the decompression area from which the flap had been removed.

There slowly developed complete right hemiplegia. On two occasions the dilated ventricle was opened. On the first occasion, when it was noted that the left foramen of Monro was blocked, all the choroid plexus that could be seen was coagulated. The second time an unsuccessful attempt was made to reopen the foramen of Monro; it was necessary to make a false opening into the third ventricle, in which a rubber dam was placed to keep the drainage tract open. This, however, failed to relieve the tension.

An encephalogram showed a block at the base of the brain. After indecision on the part of the parents, a straight line suboccipital craniectomy was performed, and adhesions were broken up between the dura and the rim of the basilar cistern.

The patient progressed fairly well after this procedure for four or five days, and then the left ventricle slowly refilled. It was tapped on two successive days; on the first occasion 150 cc. of yellowish fluid was withdrawn and on the second 100 cc. After this the temperature rose, and the patient died about three days later, on Jan. 10, 1935.

CASE 8.—*A youth sustained a depressed fracture of the skull at the age of 17, and subsequently there developed jacksonian convulsions on the right side and generalized convulsions. At operation a cyst was observed. The first operation for excision of the scar did not relieve the convulsions. The second radical operation resulted in death from shock and hyperthermia.*

History.—J. Z., a white man aged 22, was first admitted to the Graduate Hospital on Nov. 26, 1932, and again on April 12, 1933; he died on April 29, 1933. The family history was without significance. The patient was in good health until the age of 17 years, when he sustained a depressed fracture of the skull in the left frontal region. Subsequently there developed convulsions beginning on the right side of the body and becoming generalized. The convulsions were accompanied by loss of consciousness and occurred at monthly intervals.

Examination.—There were no significant findings, except a depression over the left frontal bone. There was slight weakness of the right arm.

Laboratory Data.—Urinalysis, a blood count, blood chemistry determinations, Wassermann tests of the blood and studies of the spinal fluid gave normal results.

Roentgen Examination (Nov. 28, 1932, by Dr. George E. Pfahler).—Examination of the skull showed evidence of past trauma and loss of bone in the left frontal area. This extended from the midline toward the left for a distance of 5 cm. and was rather triangular; the bony margins were ragged. A lateral view showed evidence of depression of the inner table. There appeared to be a marked reparative process in the area of the left frontal sinus, the sinus practically being obliterated by the thickening and condensation of bone.

An encephalogram suggested, but inconclusively, owing to technical difficulties, the presence of a cyst.

First Operation.—On December 8, with the patient under anesthesia induced with tribromethanol in amylene hydrate and procaine hydrochloride, which had to be reenforced with ether, one of us (F. C. G.) made an incision from the outer canthus of one eye to that of the other, running through a point 2 inches (5 cm.) above the hair line. The skin was turned down over the eyebrows. There was slight difficulty in dissecting the skin from the area of the defect, but finally it was possible to isolate the edges of the lesion. It was a curious L-shaped fracture and extended much farther downward than had been suspected. A loose piece of bone directly in the midline was removed with some hesitation, because of the fear that it might involve the sinuses. With the Bovie instrument

the scar tissue which lay in the defect was removed. This led to a large cyst, containing probably 30 cc. of fluid. In exploring the cyst an opening was made accidentally into the ventricle. It is not believed that the cyst originally communicated with the ventricle, for if it had done so it would have shown in the roentgenogram. Difficulties were encountered because of the opening into the ventricle, and there was no way of securing a water-tight closure. There seemed to be no dura around the edges of the defect. A graft was taken from the external table of the left temporoparietal region, after extending the straight midline incision backward from the tip of the curved incision. There was difficulty in securing the graft. However, holes were made with the Sherman drill, and the graft was wired below to the periosteum of the skull. The wound was closed as usual in layers, with stab wound drainage behind the posterior limb of the flap. The scar on the forehead was excised and a good skin apposition obtained. The patient was given 300 cc. of blood while on the table, for the procedure was long, tedious and rather bloody.

Course.—The patient was discharged on December 22 in a fair condition. However, the convulsions became more frequent, and he was readmitted to the hospital on April 12. The roentgenograms on April 21 and April 22 were read as follows: The area of the operation was characterized by cleancut edges of bone, and there was no marked depression of any of the fragments. There was then visible a strange area of rarefaction, of increased radiolucence in a localized pool-like area over the left parietal lobe, just beside the midsagittal plane. It measured about 8 cm. in diameter. We are at a loss to explain the cause of this appearance, but it suggested the presence of air or of air and fluid. A film of the skull in the erect position should be made to see whether one can determine a fluid level.

Additional examination made with the skull in the erect position failed to reveal definitely the presence of a fluid level in the area of rarefaction already described. There was a line in the most dependent portion of the shadows, which was rather straight and might have been a fluid level, but it was not sharp enough for this assertion to be made unequivocally.

Second Operation.—On April 29, with tribromethanol and local anesthesia, the old incision across the front of the head was reopened. After considerable difficulty the bone flap was turned back; it included the bone around the edge of the previous defect, so that the graft was lifted off without breaking it. The only unforeseen incident during this stage of the operation occurred when the bone flap was turned back, the orbital ridge being used as the base of the flap: The bone broke into the frontal sinus, tearing the mucous membrane. Both the right and the left frontal lobe were exposed, the left to a large extent and the right to a distance of about 1 inch across the midline. It would probably be more accurate to say that the area was exposed in which the frontal lobes had been, for the tip of the right frontal lobe was replaced by a large extradural cystic area, which did not communicate with the ventricle or subarachnoid spaces and which therefore was not visualized on the encephalogram. The left frontal lobe was replaced by a porencephalic cyst, which was known to be present.

The cyst was opened, exposing the anterior horn of the left ventricle, with the choroid plexus in place. The choroid plexus was coagulated to as great an extent as possible, and the large vessel which ran into it was clipped. It was then debated whether the frontal lobe should be excised, as it was obvious that both frontal lobes would have to be removed for a distance of about 1 inch at least to pass outside the scar tissue. It was found that the tips of both lobes

could be elevated without particular difficulty and with little or no bleeding. All the scar tissue in this region was removed; it included the tips of both frontal lobes. The only bleeding came from an inadvertent cut into the superior longitudinal sinus in crossing the midline, and this was promptly controlled with hemostats and was secured permanently with clips.

Although not much blood was lost, the patient reacted badly to the severe trauma to the frontal part of the brain. The pulse rate reached 150, and the blood pressure disappeared; 500 cc. of 5 per cent dextrose and 50 cc. of 50 per cent dextrose were given. This restored the condition. By the time hemostasis was completed in the wound, which was not particularly difficult, the pulse rate was down to 120, and the blood pressure had returned to 80 systolic and 60 diastolic.

A piece of dura was placed over the defect of the mucous membrane of the frontal sinus and the bone flap turned down over this defect, holding the dural graft in place. After complete hemostasis of the cutaneous flap, it was closed as usual in layers, with stab wound drainage behind the posterior limb of the flap. The patient was returned to the ward in fair condition. He died of operative shock and hyperthermia on the same day.

CASE 9.—*A man whose birth and early development were normal had experienced weakness of the right extremities at about 4 years of age and jacksonian fits on the right side at the age of 10 years. There were right hemiplegia, right hemianesthesia and right hemianopia. The diagnosis of porencephaly was confirmed by encephalography. Convulsions were diminished by the use of phenobarbital.*

History.—E. S., a Negro aged 20 years, was admitted to the Graduate Hospital on Oct. 14, 1932, complaining of convulsions on the right side. The family history was without significance. He was born at full term, with normal delivery; he walked and talked before the age of 2 years. He had pneumonia, without complications or sequelae, at the age of 3 years. In the following year he had an acute illness and paralysis of the right extremities, which was diagnosed as acute anterior poliomyelitis. He began to have convulsions at the age of 10 years and had had them at irregular intervals of about one week since. The convulsions usually began with the feeling that "the blood clotted in the right arm and leg," which was followed by twitching of the right arm and later of the leg. The movements did not extend to the rest of the body, but the patient became weak in all limbs and could not stand. There was no loss of consciousness with the attacks or history of petit mal. There was occasional incontinence of urine during the attacks. The patient had never been able to be employed usefully.

General Somatic Examination.—The results were normal except that the head was smaller than average.

Neurologic Examination.—Psychologic tests revealed mental deficiency.

Cranial Nerves: The sense of smell was normal. The fundi showed no definite abnormalities; acuity of vision in the right eye was 6/12 and in the left 6/15; there was right homonymous hemianopia, with sparing of central vision. There was narrowing of the right palpebral fissure; slight but persistent lateral nystagmus occurred on deviation of the eyes, and the pupils were equal and regular but responded poorly to light. There was slight hypalgesia of the right side of the face, unaccompanied by corneal analgesia. There was definite weakness of the right lower part of the face on volitional and emotional innervation. Hearing was normal bilaterally; Bárány tests indicated a lesion in the supratentorial region (absence of shock reaction), probably on the left side (perverted nystagmus from the left horizontal canal on douching). All other cranial nerves were normal.

Upper Extremities: The right arm was smaller than the left (22 cm. and 29 cm. in circumference, respectively). The musculature in both extremities was firm, and there was no fibrillation. Flexion and extension at the elbow were fair. There were weakness of pronation and supination and almost complete paralysis of the right hand. There were no definite disturbances of tonus. The biceps and triceps reflexes were hyperactive on the right, as compared with those on the left. There was marked diminution of all forms of sensation on the right side. Objects placed in the right hand could not be identified.

Lower Extremities: The right thigh (50 cm. in circumference) and calf (30 cm.) were smaller than the left (53 cm. and 32 cm., respectively). There was no difference in the length of the limbs. The musculature was firm and without fibrillations, but there was spasticity in the right lower extremity. No weakness appeared in tests of individual muscle groups, but in walking there were a decided limp on the right side and scoliosis. The knee and ankle reflexes were exaggerated bilaterally, but more on the right than on the left; there was no clonus or Babinski sign. There was slight impairment of sensation in all modalities in the right lower extremity. The heel to knee test showed awkwardness on the right.

Trunk: There was slight diminution in all forms of sensation on the right. The abdominal and cremasteric reflexes were active bilaterally. There was no trunkal weakness or dyssynergia. There was dorsolumbar scoliosis.

Laboratory Data.—Urinalysis, a blood count, determinations of the urea nitrogen and sugar of the blood, Wassermann tests of the blood and complete studies of the spinal fluid gave normal results.

Roentgen Examination (Dr. George E. Pfahler).—The skull was of the microcephalic type, with generally thickened walls. The suture, vascular and convolutional markings were about average. There was no roentgenographic evidence of increased intracranial pressure. The pineal body was not calcified. The sella turcica was of small size, measuring approximately 6 mm. anteroposteriorly and 5 mm. in depth. There was no definite evidence of erosion or tumor formation. The sphenoid sinuses were well delineated and were not encroached on.

Encephalograms showed the right ventricle to be apparently normal, but an unusual dense area occupied approximately the central area of the brain and was about 2.5 cm. in diameter. In the postero-anterior view this was slightly displaced to the right of the median line. The striking feature of the encephalogram, however, was an enormous cavity occupying the general region of the left ventricle but extending outward as far as the lateral wall of the skull. The cavity was approximately 7 cm. in a vertical and 5.5 cm. in a lateral diameter. This extended downward as far as the middle fossa and must have represented extensive atrophy of this portion of the brain, covering a total area about the size of a goose-egg.

Course.—Operation was suggested, but permission was refused. The patient has received 1½ grains (0.0972 Gm.) of phenobarbital at bedtime. He has shown considerable improvement in that the convulsions have become infrequent, occurring from about two to four times each year.

SUMMARY AND CONCLUSIONS

Nine cases of porencephaly are reported. The encephalograms revealed positive findings in all instances. In eight instances the diagnosis was verified at operation; one patient refused operation. The cyst was located in the left cerebral hemisphere in eight of the nine cases. In eight of the nine cases there were evidences of abnormalities which had

existed since early childhood, the most important being lack of development of one half, or part of one half, of the body, accompanied by motor weakness and jacksonian convulsions in all cases and by hemianesthesia, hemianopia, atrophy of the optic nerve and generalized convulsions in some. In one case a cyst and convulsions developed at the age of 17 years; in this instance no lack of development in the neuromuscular apparatus was shown. Of the eight patients on whom operation was performed two died. Of the six surviving patients three had complete relief from convulsions, while the others showed marked improvement.

The existence of unilateral lack of development combined with motor weakness, sensory disturbances and jacksonian convulsions suggests the presence of porencephaly and should lead to air studies and an attempt at surgical correction.

No adequate explanation can be offered for the predominance of a left cerebral lesion, the occurrence of the convulsions or the relatively little dysfunction in cases of a large lesion of the brain of this sort. This study does not help in establishing the etiology of the condition in these cases, except to indicate that it probably had its inception early in life.

Technical and Occasional Notes

GALVANIC FALLING IN CLINICAL USE

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Galvanic falling, reported over a hundred years ago,[1] has not been utilized as a clinical procedure for testing labyrinthine functions, as have the caloric and rotation tests, because of inconsistent results. Disturbance of the normal posture of a person or of an experimental animal by stimulation of the region of the ear with the galvanic current has been reported by many investigators (Ritter, cited by Stern [2]), Purkinje, Remak, Brenner, Hitzig,[1] James,[3] Pollak [4] and Babinski.[5] Hitzig in 1871, sixty-eight years after the early report of Augustine and almost fifty years after Purkinje's work on the galvanic falling reaction (cited by Hitzig [1]), noted that the direction of the falling obtained on closure of the galvanic circuit was uniformly toward the anodal electrode. Early investigators considered the reactions to be due to central stimulation, principally of the cerebellum. Breuer [6] localized the reactions obtained by galvanic stimulation of the vestibular system by constructing two circuits, one through the cerebellum and the other through the labyrinth. Only the labyrinthine circuit gave the typical reactions. Jensen,[7]

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1. Hitzig, E.: Ueber die beim Galvanisieren des Kopfes entstehenden Störungen der Muskelinnervation und der Vorstellung vom Verhalten im Raume, in Untersuchungen über das Gehirn, Berlin, A. Hirschwald, 1874, p. 196.

2. Stern, William L.: Die Literatur über die nichtakustische Funktion des innern Ohres, Arch. f. Ohrenh. **39**:248, 1895.

3. James, William: Sense of Dizziness in Deaf Mutes, Am. J. Otol. **4**:239, 1882.

4. Pollak, J.: Ueber den galvanischen Schwindel bei Taubstummen und seine Beziehungen zur Funktion des Ohrenlabyrinthes, Arch. f. d. ges. Physiol. **54**:188, 1893.

5. Babinski, J.: Sur les mouvements d'inclination et de rotation de la tête dans le vertige voltaïque, Compt. rend. Soc. de biol. **55**:513, 1903; Sur le mecanisme du vertige voltaïque, ibid. **55**:350, 1903. Babinski, J.; Vincent, C., and Barré, A.: Vertige voltaïque: Nouvelles recherches expérimentales sur le labyrinthe du cobaye, Rev. neurol. **21**:410, 1913; Vertige voltaïque: Perturbation dans les mouvements des globes oculaires à la suite de lésions labyrinthiques expérimentales, ibid. **21**:253, 1913.

6. Breuer, J.: Neue Versuche an den Ohrbogengängen, Arch. f. d. ges. Physiol. **44**:135, 1889.

7. Jensen, P.: Ueber den galvanischen Schwindel, Arch f. d. ges. Physiol. **64**:182, 1896.

Beyer and Lewandowsky [8] and Kny [9] individually confirmed Breuer's work by obtaining the galvanic reactions after extirpation of the cerebellum.

Controversy arose as to whether the labyrinth or the retrolabyrinthine structures are stimulated by a galvanic current. The literature contains much evidence in favor of each location.[10] Ewald [10l] was the first to demonstrate in pigeons that if a small amount of galvanic current is used spread of current can be avoided, and that the reactions thus obtained are entirely of labyrinthine origin. Later Jensen [7] with pigeons, Babinski [5] with pigeons, dogs and guinea-pigs, Köllner and Hoffmann [10m] with rabbits and Blau [3] with cats confirmed Ewald's findings.

Galvanic nystagmus has been much more frequently observed and reported than galvanic falling. This nystagmus is small and inconstant, frequently requiring convex lenses for its observation.

James [3] tested forty-three deaf pupils with a strong current and reported nystagmus, vertigo, falling, stinging of the skin, subjective noises, flashes of light and occasionally cerebral confusion on galvanic stimulation of the mastoid. Pollak [4] performed tests on fifty normal persons and eighty-two deaf-mutes. He noted the characteristic falling, nystagmus and vertigo in normal persons, using from 5 to 13 milli-

8. Beyer, H., and Lewandowsky, M.: Experimentelle Untersuchungen am Vestibularapparat von Säugetieren, Arch. f. Physiol., 1906, p. 451.

9. Kny, E.: Untersuchungen über den galvanischen Schwindel, Arch. f. Psychiat. **8**:637, 1887.

10. (*a*) Dohlman, G.: Experimentelle Untersuchungen über die galvanische Vestibularisreaktion, Acta oto-laryng., supp. 8, 1929, pp. 1-48. (*b*) Marx, H.: Ueber den galvanischen Nystagmus, Ztschr. f. Ohrenh. **63**:201, 1911. (*c*) Strehl, H.: Beiträge zur Physiologie des innern Ohres, Arch. f. d. ges. Physiol. **59**:207, 1895. (*d*) von Cyon, E.: Das Ohrlabyrinth als Organ der mathematischen Sinne für Raume und Zeit, Berlin, Julius Springer, 1908. (*e*) Högyes, E.: Ueber den Nervenmechanismus der assozierten Augenbewegungen, Monatschr. f. Ohrenh. **46**:1027, 1912. (*f*) Kubo, I.: Ueber die vom Nervus acusticus ausgelösten Augenbewegungen, Arch. f. d. ges. Physiol. **114**:143, 1906. (*g*) Kuffler, O.: Ueber elektrische Reizung des Nervus viii und seiner Endorgane beim Frosch, ibid. **83**:212, 1901. (*h*) Rhese, H.: Ueber die traumatische Läsion der Vestibularisbahn insbesondere über den Sitz der Läsion, Ztschr. f. Ohrenh. **70**:262, 1914. (*i*) Mann, L.: Ueber die galvanischen vestibulären Körperreflexe und Reaktionsbewegungen beim Menschen, Klin. Wchnschr. **2**:1802, 1923. (*j*) Wilson, J. C., and Pike, F. H.: The Effects of Stimulation and Extirpation of the Labyrinth of the Ear and Their Relations to the Motor System, Phil. Tr., London **203**:127, 1913. (*k*) Bárány, R.: Physiologie und Pathologie des Bogengang-Apparates beim Menschen, Leipzig, F. Deuticke, 1907, p. 34. (*l*) Ewald, Richard J.: Die Abhängigheit des galvanischen Schwindels vom inneren Ohr, Centralbl. f. d. med. Wissensch. **42**:753, 1890. (*m*) Köllner, H., and Hoffmann, P.: Der Einfluss des Vestibularapparates auf die Innervation der Angenmuskeln, Arch. f. Augenh. **92**:727, 1923. (*n*) Blau: Experimentelle Studien über den galvanischen Nystagmus, Ztschr. f. Ohrenh. (supp.) **69**:6, 1913. (*o*) Alexander, G., and Kreidl, A.: Ueber die Beziehungen der galvanischen Reaction zur Angeborenen und erworbenen Taubstummheit, Arch. f. d. ges. Physiol. **89**:475, 1902. (*p*) Mygind, S. H.: Vestibular Examinations in Normal Individuals, Acta oto-laryng. **19**:527, 1924.

amperes of current. Those who failed to react to rotation tests were inactive to as high as 20 milliamperes of galvanic current. Babinski [5] noted falling toward the anode and mild dizziness in normal persons. Alexander and Kreidl [10o] reported anodal falling in sixty-four deaf-mutes with active labyrinths. Nystagmus was not reported. Mackenzie,[11] in collaboration with Alexander, noted both falling and nystagmus but recorded principally the latter. The general impression created by the investigations with galvanic current was that when a small amount of current is used the stimulation is limited to the labyrinth. In testing for galvanic falling some investigators had the patient stand upright with the feet together or the heel of one foot in front of the toe of the other. Mygind [10p] used the sitting position. Wodak and Fischer [12] had the patient stand upright with the feet together, the arms extended horizontally forward and the eyes closed. Galvanic stimulation of the mastoid produced a slow falling reaction, which they termed the "discobolus reaction" because the position assumed resembled that of a discus thrower. Varying with the individual investigators, from 3 to 20 milliamperes of galvanic current has been used to produce falling. Confusing, contradictory clinical evidence has been reported; for example, Dundas-Grant [13] reported galvanic nystagmus in subjects inactive to caloric and rotation tests. Koch,[14] Vogel [15] and Schur [16] reported that galvanic nystagmus confirmed caloric and rotation findings. MacKenzie [11] considered the galvanic reactions constant, while many others, including Mygind,[10p] Bárány,[10k] Dundas-Grant [13] and Dohlman,[10a] differed with him. Junger [17] failed to confirm the results of Wodak and Fischer.

The objection to the clinical application of galvanic falling has been the inconsistent results, which were caused by: (1) voluntary interference by the patient, (2) large amounts of current, which produced spread reactions, and (3) pain, which besides being disagreeable produced movements in addition to those induced by vestibular stimulation.

I believed that consistent, accurate galvanic falling reactions would prove a valuable adjunct to the caloric and rotation tests. If the disagreeable phenomena associated with these tests are avoided, galvanic falling may in some instances supplant the usual labyrinthine tests.

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11. MacKenzie, G. W.: Klinische Studien über die Funktionsprüfung des Labyrinthes mittelst galvanischen Stromes, Arch. f. Ohrenh. **77**:1, 1908.

12. Wodak, E., and Fischer, M. H.: Die "vestibulären Körperreflexe" und die "Fall Reaktion," Arch. f. d. ges. Physiol. **202**:525, 1924.

13. Dundas-Grant, J.: Remarks on the Various Labyrinth Tests, M. Press **113**:50, 1922.

14. Koch, J.: Beitrag zur Frage der Entstehung, Beurteilung und Behandlung von Erkrankungen mit anfallsweise auftretendem Vestibularschwindel (Oktavnskrisen), Arch. f. Ohren-, Nasen- u. Kehlkopfh. **134**:314, 1933.

15. Vogel, C.: Ueber den Nachweis des latenten Spontannystagmus, Ztschr. f. Laryng., Rhin., Otol. **22**:202, 1932.

16. Schur, E.: Studien über das statische Organ normaler Säuglinge und Kinder, Ztschr. f. Kinderh. **32**:227, 1922.

17. Junger, I.: Die Reaktionsbewegungen des Körpers bei galvanischer Prüfung des Labyrinth, Ztschr. f. Hals-, Nasen- u. Ohrenh. **3**:225, 1922.

I hoped that the additional data accumulated as a result of a large series of galvanic falling tests would lead to localization of lesions of the vestibular arc, which had previously been obscure.

METHODS OF INVESTIGATION

Luhan[18] reported deviations of the upper extremities induced by galvanic stimulation of the region of the ear when the arms were placed in a suspended platform. I repeated tests with his method, but it was not easily adaptable for clinical observations as a routine. The use of the method of Wodak and Fischer was limited in my hands to a few persons. The other positions suggested gave inconsistent results, owing to the large amount of current necessary.

To remove voluntary interference during galvanic stimulation of the ear, I placed the patient on a wooden platform supported by a narrow board, arranged to act as a fulcrum. I have termed this platform apparatus a balance board, and its use has removed all the objections present with other methods. The method is simple and easily adapted to general clinical use and gives accurate results. Only a small amount of current is necessary. No disagreeable phenomena are produced. The galvanic falling reaction obtained with the balance board is easily recognized. In 1933, at a meeting of the Society of Neurologic Surgeons, I demonstrated galvanic falling with the use of a balance board.

The balance board consists of a platform 16 inches (41 cm.) wide, 21 inches (53 cm.) long and ¾ inch (1.9 cm.) thick, under which is a fulcrum 3½ inches (8.9 cm.) wide and ⅞ inch (2.2 cm.) high. Circular electrodes covered with moist cloth are used. The patient is placed in the normal standing posture on the balance board, which is constructed so that a normal person can maintain his equilibrium without effort. For unilateral stimulation one electrode is placed on the mastoid and the other on the sternum. Care is taken that the mastoid electrode does not touch the auricle, which is painful to galvanic stimulation. Usually from 0.5 to 2 milliamperes of current is used; only rarely as high as 5 milliamperes is required for normal persons. Closure of the circuit produces lowering of the platform on the anodal side. When over 5 milliamperes of current is used, pain of varying degrees results.

RESULTS

I tested one hundred and twenty-five persons (eighty-three of whom were normal) for galvanic falling reactions with the use of the balance board. The normal persons were members of the department, medical students and patients from the clinic. Each of the eighty-three normal persons reacted on closure of the galvanic circuit by lowering the platform on the anodal side. There were no doubtful reactions. Vertigo was absent in most instances or only slight in a few cases, and it was not a factor in falling. When present it was not rotatory. The subjects experienced a sensation of being pushed or pulled over.

The forty-two pathologic subjects were patients of Drs. Lewis J. Pollock and Loyal Davis and myself and from the clinic. They included: fourteen patients with "idiopathic epilepsy" and one with nerve deafness, all of whom were active to the caloric test; six who had undergone mastoidectomy, with cochlear defects; one with bilateral suppurative otitis media, who was active to rotation and caloric tests, and patients with one of the following conditions: acute otitis media, otitis externa,

18. Luhan, J.: A Study of Postural Reflexes in Man, Master's Thesis, Chicago, Northwestern University Medical School, 1932.

myasthenia gravis, migraine and verified cerebellar tumor. All these twenty-seven patients fell toward the anode on closure with the usual amount of current. Four patients who were hyperactive to the caloric test and reacted with galvanic falling to only a small amount, 0.5 milliamperes, of current had, respectively: labyrinthine fistula, a condition suspected to be an intracranial lesion, verified supratentorial tumor and recently healed serous labyrinthitis. The remaining ten pathologic subjects gave inactive reactions to the usual labyrinthine tests. They included two patients with chronic suppurative otitis media and cochlear deafness, one with a preexisting basilar skull fracture, one with a tumor of the cerebellopontile angle on whom operation had been performed and six with cochlear deafness, which followed an infectious disease or was of unknown cause. Patients with both labyrinths dead failed to react to galvanic stimulation when as much as 20 milliamperes was used. In patients who had only one inactive labyrinth the following reactions took place: When the anodal or cathodal electrode was placed on the mastoid of the side of the dead labyrinth and the other electrode on the sternum, no falling took place with from 15 to 20 milliamperes. With the anodal electrode on the mastoid on the side of the active labyrinth and the cathode on the sternum, closure of the circuit with a small amount of current caused lowering of the platform on the anodal side. When the cathode was placed on the intact side and the anode on the sternum, falling took place toward the diseased side. Falling in the direction opposite to that which occurred when the circuit was closed followed opening of the circuit. These reactions in patients with one dead labyrinth indicate that a single labyrinth can be stimulated when one electrode is placed on the mastoid and the other on the sternum and also that each labyrinth may be stimulated negatively or positively by the galvanic current. Opening the circuit produces falling toward the cathode.

CONCLUSIONS

I have described a clinical method for testing the integrity of the vestibular arc by observing the falling reaction produced by a galvanic current when the patient stands on the platform of a balance board. This test has given us constant and reliable results in both normal and pathologic subjects as has caloric stimulation. I believe that the results obtained with this clinical application of the galvanic falling reaction will be found reliable by any one using this method. The galvanic falling reaction with the balance board produces no disagreeable symptoms and can be repeated in a short time with no discomfort to the patient, and on each occasion with the same result.

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SPECIAL ARTICLES

CHEMICAL MEDIATION OF NERVE IMPULSES

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The first intimation of the chemical mediation of nerve impulses was given by Elliott [1] (1905). He observed that the structures innervated by sympathetic nerves responded in a characteristic manner to epinephrine long after these nerves had been cut and had undergone degeneration. If a structure, smooth muscle, for example, contracted in response to sympathetic impulses it contracted in response to epinephrine, and if sympathetic impulses caused relaxation, the response to epinephrine also was relaxation. It was obvious that epinephrine did not affect any part of the peripheral nerves, for they had undergone degeneration. On the basis of these observations Elliott suggested that the sympathtetic nerve impulse arriving at a smooth muscle cell might liberate epinephrine in the cell and that this epinephrine acts as a chemical mediator in the process of stimulation. This would explain the manner in which epinephrine from the adrenal gland mimics the action of sympathetic impulses.

It is well known that in some smooth muscle cells sympathetic impulses and injection of epinephrine cause contraction and in others relaxation. These impulses also can be produced artificially by electric shock. The question then arose in the minds of physiologists, as expressed by Cannon [2] (1934): "How, then, may these quite contrary effects of the same agents be explained?" In 1905 Langley [3] suggested that in reacting cells there existed an excitatory and an inhibitory receptive substance. He concluded that on reaching the cell epinephrine acts according to the kind of receptive substance present; if it unites

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Review prepared while in the Department of Neurology of the Mayo Clinic and presented at the neurologic seminary, Dec. 19, 1935.

1. Elliott, T. R.: The Action of Adrenalin, J. Physiol. **32**:401-467 (July 13) 1905.

2. Cannon, W. B.: The Story of the Development of Our Ideas of Chemical Mediation of Nerve Impulses, Am. J. M. Sc. **188**:145-159 (Aug.) 1934.

3. Langley, J. N.: On the Reaction of Cells and of Nerve-Endings to Certain Poisons, Chiefly as Regards the Reaction of Striated Muscle to Nicotine and to Curari, J. Physiol. **33**:374-413 (Dec. 30) 1905.

with the excitatory substance contraction results and if with the inhibitory substance relaxation results.

In 1896 Bottazzi [4] noted the resemblance between the inhibition of the heart induced by potassium salts and that induced by vagal stimulation. Martin [5] (1904) confirmed this work, and Howell [6] (1906) concluded that the vagal impulses act indirectly by increasing the amount of potassium salts in the cardiac tissue. Later, Howell and Duke [7] (1908) observed increase in the potassium content of Locke's solution perfused through an isolated mammalian heart after vagal stimulation. From this they concluded that the cardio-inhibitory influence of the vagus nerve is dependent on the direct action of diffusible potassium compounds which vagal impulses set free. This was apparently the end of the search, and for a number of years the aforementioned views were accepted by a large number of physiologists and were taught to students as fact.

A year after Howell's work, Dixon and Hamill [8] (1909) drew attention to the similar actions of muscarine and vagal stimulation on the heart; both are completely antagonized by atropine. They suggested that excitation of a nerve induces the local liberation of a hormone which causes specific activity by combination with a constituent of the end-organ, muscle or gland. This theory is essentially the same as that proposed by Elliott except that the interest of Dixon and Hamill was in muscarine and vagal stimulation and that of Elliott was in epinephrine and sympathetic stimulation.

In 1906 Hunt and Taveau [9] noted in aqueous extracts of adrenal glands a substance which reduced blood pressure and which, on chemical treatment, disappeared as the content of choline increased. They finally produced an unstable ester, acetylcholine, which proved to be one hundred thousand times as active as choline in causing a fall in blood pressure and to have one hundred times the effect in that direc-

4. Bottazzi, Phil.: Sur le mecanisme d'action des seis de potassium sur le coeur: Contribution à la doctrine de l'inhibition, Arch. de physiol. norm. et path. **8**:882-892, 1896.

5. Martin, E. G.: The Inhibitory Influence of Potassium Chloride on the Heart, and the Effect of Variations of Temperature upon This Inhibition and upon Vagus Inhibition, Am. J. Physiol. **11**:370-393 (July) 1904.

6. Howell, W. H.: Vagus Inhibition of the Heart in Its Relation to the Inorganic Salts of the Blood, Am. J. Physiol. **15**:280-294 (Feb.) 1906.

7. Howell, W. H., and Duke, W. W.: The Effect of Vagus Inhibition on the Output of Potassium from the Heart, Am. J. Physiol. **21**:51-63 (Feb.) 1908.

8. Dixon, W. E., and Hamill, P.: The Mode of Action of Specific Substances with Special Reference to Secretin, J. Physiol. **38**:314-336 (March 22) 1909.

9. Hunt, Reid, and Taveau, R. de M.: On the Physiological Action of Certain Cholin Derivatives and New Methods for Detecting Cholin, Brit. M. J. **2**:1788-1791 (Dec. 12) 1906.

tion that epinephrine has in causing a rise. Dale[10] (1914), working with certain extracts of ergot, observed pharmacologic changes that resembled those produced by muscarine and found the responsible agent to be acetylcholine. He injected acetylcholine and observed a "pronounced vagus-like inhibition of the heart, and various other effects of stimulating nerves of the cranial and sacral divisions of the autonomic nervous system—secretion of saliva, contraction of the esophagus, stomach, and intestine, and of the urinary bladder."

Then came the World War, and seven years passed before the thread of this story was again picked up. In 1921 Loewi,[11] by the simplest experiment imaginable, proved conclusively that nerve impulses are transmitted by a chemical mediator. By using isolated hearts of frogs, he showed that vagal inhibition of one heart released into the fluid filling this heart a substance which when brought into contact with the other heart transferred to it the effect of the vagus nerve and that sympathetic stimulation released an accelerator substance that could be detected similarly. When the action of a vagus or sympathetic nerve fiber was paralyzed by atropine or ergotamine, respectively, the chemical transmitter of nervous activity was still released. Cannon (1934) related the story of how Loewi was suddenly awakened from a sound sleep with the idea of this ingenious experiment clearly in his mind. He wrote the plan on a piece of paper and went to sleep again. The next morning he was unable to read his crude "sleepy writing" and was unconscious of any dream he might have experienced. The next night "he again awoke with vivid revival of the incidents of the previous illumination, and after this experience he remembered in his waking state both occasions." Loewi and Navratil[12] (1926) further found that the chemical substance mediating the effect of the vagus nerve is an unstable choline ester, that the heart contains an esterase which rapidly destroys this substance and that physostigmine inhibits the action of this esterase, that is, it retards the decomposition of acetylcholine.

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10. Dale, H. H.: The Action of Certain Esters and Ethers of Choline, and Their Relation to Muscarine, J. Pharmacol. & Exper. Therap. **6**:147-190 (Nov.) 1914; The Occurrence in Ergot and Action of Acetyl-Choline, J. Physiol. **48**: iii-iv (Jan. 24) 1914.

11. Loewi, O.: Ueber humorale Uebertragbarkeit der Herznervenwirkung, Arch. f. d. ges. Physiol. **189**:239-242, 1921.

12. Loewi, O., and Navratil, E.: Ueber humorale Uebertragbarkeit der Herznervenwirkung: X. Ueber das Schicksal des Vagusstoffs, Arch. f. d. ges. Physiol. **214**:678-688, 1926; Ueber humorale Uebertragbarkeit der Herznervenwirkung: XI. Ueber den Mechanismus der Vaguswirkung von Physostigmin und Ergotamin, ibid. **214**:689-696, 1926.

In 1921 Cannon and Uridil[13] reported that stimulation of the splanchnic nerve causes the denervated heart to beat faster if the adrenal glands are intact and that the same stimulus, even after removal of these glands, retains this effect, but in less marked degree.

These two noteworthy contributions led separately to the proof of chemical mediation of nerve impulses in both the sympathetic and the parasympathetic system.

SYMPATHETIC NERVOUS SYSTEM

Loewi's original evidence concerning the sympathetic system has been confirmed by Plattner[14] (1925), Samojloff[15] (1927) and Bain[16] (1932). Brinkman and van Dam[17] (1922), Külz[18] (1928) and others observed that perfusion fluid from a heart accelerated by sympathetic stimulation exerts an inhibitory effect on gastric peristalsis typical of that of epinephrine. Finkelman[19] (1930), in an ingenious experiment, showed that when an excised piece of intestine of the rabbit still supplied with its nerves (piece A) was stimulated and Ringer's solution, flowing over this piece, was allowed to drop on another strip of pulsating intestine (piece B) and the contraction of piece A was then inhibited by stimulation of its nerves, piece B was also inhibited by some new property in the solution dropping on it.

In 1929 Demoor,[20] a Belgian physiologist, unfavorably criticized nearly all the aforementioned experiments because the apparent chemical mediator had been carried by a salt solution. He contended that irrigation of these organs might create new conditions of existence for the tissues, such as changed permeability, which do not occur in the normal state. Cannon and Uridil[13] (1921) had been the only workers to demonstrate that the substance could be carried by the blood

13. Cannon, W. B., and Uridil, J. E.: Studies on the Conditions of Activity in Endocrine Organs: VIII. Some Effects on the Denervated Heart of Stimulating the Nerves of the Liver, Am. J. Physiol. **58**:353-364 (Dec. 1) 1921.

14. Plattner, Friedrich: Eine Bestätigung der humoralen Uebertragbarkeit der Herznervenwirkung, Ztschr. f. Biol. **83**:544-546, 1925.

15. Samojloff, A.: Die Aktionsströme des Froschherzventrikels bei hormonaler Vagusreizung, Arch. f. d. ges. Physiol. **217**:582-597, 1927.

16. Bain, W. A.: A Method of Demonstrating the Humoral Transmission of the Effects of Cardiac Vagus Stimulation in the Frog, Quart. J. Exper. Physiol. **22**:269-274 (Dec.) 1932.

17. Brinkman, R., and van Dam, E.: Die chemische Uebertragbarkeit der Nervenreizwirkung, Arch. f. d. ges. Physiol. **196**:66-82, 1922.

18. Külz, Fritz: Zur Humoralphysiologie des Froschherzens, Arch. f. exper. Path. u. Pharmakol. **134**:252-256, 1928.

19. Finkelman, B.: On the Nature of Inhibition in the Intestine, J. Physiol. **70**:145-157 (Sept. 18) 1930.

20. Demoor, J.: Le réglage humoral dans le cœur, Ann. de physiol. **5**:42-129 (Jan.) 1929.

stream. In 1931 Cannon and Bacq [21] again reported that a substance is carried in the blood stream from a stimulated region and that its effect mimics the effects of sympathetic impulses and produces elsewhere effects typical of those of epinephrine.

Cannon, Lewis and Britton [22] in 1926 devised a method of separating the heart surgically from the central nervous system while leaving the organism otherwise in a normal state. Under these conditions the heart, although not subject to nervous control, remains very sensitive to a minute increase of epinephrine in the circulating blood, and a rapid rise in cardiac rate, up to 100 beats a minute, follows such stimuli as motion, asphyxia, emotion and pain. This effect, they considered, was attributable to liberation of the adrenal medullary secretion. After extirpation of the adrenal glands they noted no immediate rise in the cardiac rate after various stimuli, but within three minutes there was a slow rise of from 25 to 30 beats a minute.

In 1931 Newton, Zwemer and Cannon [23] showed that this slow rise was not attributable to increase in blood pressure or temperature or to muscle metabolites. They further removed the adrenal medulla and cortex and all accessory chromaffin tissue, set aside the liver by cutting the hepatic nerves, extirpated the abdominal portion of the sympathetic chain, removed the pituitary gland and disconnected the thyroid and the parathyroid glands from the spinal cord by removing the cervical portion of the sympathetic chain, and still this mysterious acceleration persisted. The only sympathetic nerves left were a few short strands in the lower part of the thorax. These were removed, and the acceleration following the application of various stimuli ceased.

Later, Cannon and Bacq [21] (1931) observed that after stimulation of the lower part of the abdominal portion of the sympathetic chain of animals in which the heart had been denervated the hairs of the tail rose, and in two minutes there was a marked rise in blood pressure, and in three minutes, an increase in cardiac rate. If the blood flow into and out of the tail was blocked, the same stimulus had no effect

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21. Cannon, W. B., and Bacq, Z. M.: Studies on Conditions of Activity in Endocrine Organs: Hormone Produced by Sympathetic Action on Smooth Muscle, Am. J. Physiol. **96**:392-412 (Feb.) 1931.

22. Cannon, W. B.; Lewis, J. T., and Britton, S. W.: Studies on Conditions of Activity in Endocrine Glands: XVII. A Lasting Preparation of the Denervated Heart for Detecting Internal Secretion, with Evidence for Accessory Acceleration Fibers from the Thoracic Sympathetic Chain, Am. J. Physiol. **77**:326-352 (July) 1926.

23. Newton, H. F.; Zwemer, R. L., and Cannon, W. B.: Studies on Conditions of Activity in Endocrine Organs: XXV. The Mystery of Emotional Acceleration of the Denervated Heart, After Exclusion of Known Humoral Accelerators, Am. J. Physiol. **96**:377-391 (Feb.) 1931.

until the block had been removed. They further found that stimulation of sympathetic nerves to smooth muscle elsewhere than in the tail would produce the same effects on the denervated heart and on other denervated structures. It was concluded from these brilliant experiments that such excitation causes the affected cells to liberate a substance into the blood stream and that this substance, carried elsewhere in the body, may have effects similar to sympathetic impulses. Cannon called this substance sympathin.

Experiments followed which tended to show that sympathin is indistinguishable from epinephrine. However, in 1933 Cannon and Rosenblueth [24] proved that sympathin and epinephrine are not exactly the same. Ergotoxine blocks the influence of epinephrine on vessels that respond by constriction to sympathetic impulses, but it leaves unaffected vessels that respond by dilatation to such impulses. In this way they proved that the two materials are not the same. The difference seems to be the inability of sympathin to induce relaxation after ergotoxine. These workers also found that there exists not only a sympathin causing contraction but a substance that produces relaxation. They suggested the term sympathin E for the substance liberated by smooth muscle cells during contraction due to sympathetic stimulation and the term sympathin I for the substance liberated by smooth muscle cells during active relaxation from such impulses. They stated: "Escaping from the cells of origin, sympathin E, borne by the circulating blood, is able to cause contraction in distant smooth muscle organs which contract in response to sympathetic excitation; and sympathin I, analogously, affects smooth muscle organs which relax."

Recently, Cannon and Rosenblueth [25] (1935) produced further evidence which suggests that sympathin E, unlike epinephrine, may affect not only the dilator but the constrictor muscle of the iris.

Liu and Rosenblueth [26] (1935) showed that sympathin is also produced by reflex activation of sympathetic nerves. They also found that for the escape of sympathin into the blood a certain degree of stimulation is necessary. Dye [27] (1935), working with the cat, showed that sympathin is resistant to exhaustion and suggested that this is unlikely to occur in the process of normal bodily functions.

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24. Cannon, W. B., and Rosenblueth, A.: Studies on Conditions of Activity in Endocrine Organs: XXIX. Sympathin E and Sympathin I, Am. J. Physiol. **104**:557-574 (June) 1933.

25. Cannon, W. B., and Rosenblueth, A.: A Comparison of the Effects of Sympathin and Adrenine on the Iris, Am. J. Physiol. **113**:251-258 (Oct.) 1935.

26. Liu, A. C., and Rosenblueth, A.: Reflex Liberation of Circulating Sympathin, Am. J. Physiol. **113**:555-559 (Nov.) 1935.

27. Dye, J. A.: The Exhaustibility of the Sympathin Stores, Am. J. Physiol. **113**:265-270 (Oct.) 1935.

PARASYMPATHETIC NERVOUS SYSTEM

Mention has been made of the discovery of acetylcholine by Hunt and Taveau and of Dale's [10] observation that the action of this substance mimics the action produced by stimulating the parasympathetic nerves. A number of experiments have been reported in which transference of the parasympathetic substance by salt solutions was observed. Engelhart [28] (1931) found that the iris of the cat contains a substance resembling acetylcholine and that stimulation of the oculomotor nerve increases the quantity of this substance within the iris. Babkin, Alley and Stravracky [29] (1932) repeatedly injected physostigmine into their animals and found that if they stimulated the nerve to one submaxillary gland, thus causing it to secrete, they obtained a few seconds later a secretion from the other gland, which had been denervated. Here, the only means of communication was the circulating blood. They found further that when the vein conveying blood from the stimulated gland was closed stimulation of this gland produced no effect on the other gland. They also noted a fall in blood pressure and dilatation of the blood vessels in the denervated gland. A large number of investigators have confirmed this work, and it is generally accepted that peripheral parasympathetic effects are transmitted by liberation of acetylcholine.

Other workers have reported finding a substance, probably acetylcholine, after stimulation of the parasympathetic nerve to the salivary gland (Gibbs and Szelöczey,[30] 1932), tongue (Feldberg,[31] 1932), bladder (Henderson and Roepke,[32] 1934), stomach (Dale and Feldberg,[33] 1934) and uterus (Sherif,[34] 1935). Bacq and his co-workers [35]

28. Engelhart, Erich: Der humorale Wirkungsmechanismus der Oculomotoriusreizung, Arch. f. d. ges. Physiol. **227**:220-234, 1931.

29. Babkin, B. P.; Alley, A., and Stravracky, G., cited by Cannon.[2]

30. Gibbs, O. S., and Szelöczey, J.: Die humorale Uebertragung der Chorda tympani-Reizung, Arch. f. exper. Path. u. Pharmakol. **168**:64-88, 1932.

31. Feldberg, W.: Der Nachweis eines acetylcholinähnlichen Stoffes im Zungenvenblut des Hundes bei Reizung des Nervus lingualis, Arch. f. d. ges. Physiol. **232**:88-104, 1932.

32. Henderson, V. E., and Roepke, M. H.: The Rôle of Acetylcholine in Bladder Contractile Mechanisms and in Parasympathetic Ganglia, J. Pharmacol. & Exper. Therap. **51**:97-111 (May) 1934.

33. Dale, H. H., and Feldberg, W.: Chemical Transmitter of Vagus Effects to the Stomach, J. Physiol. **81**:320-334 (June 9) 1934.

34. Sherif, M. A. F.: The Chemical Transmitter of the Sympathetic Nerve to the Uterus, J. Physiol. **85**:298-308 (Nov. 22) 1935.

35. Bacq, Z. M.: Recherches sur la physiologie et la pharmacologie du système nerveux autonome; les esters de la choline dans les extraits de tissus des invertébrés, Arch. internat. de physiol. **42**:24-42 (Oct.) 1935; abstr., Compt. rend. Soc. de biol. **120**:243-245 (July 13) 1935. Bacq, Z. M., and Mazza, F.: Recherches sur la physiologie et la pharmacologie du système nerveux autonome; isolement de chloroaurate d'acétylcholine à partir d'un extrait de cellules nerveuses d'octopus vulgaris, Arch. internat. de physiol. **42**:43-46 (Oct.) 1935; abstr., Compt. rend. Soc. de biol. **120**: 246-247 (July 13) 1935.

(1935) have found acetylcholine in the tissue extracts of molluscs and worms and in the nerve ganglia of the octopus. By use of a denervated loop of small intestine, Bunting, Meek and Maaske [36] (1935) found that a substance resembling acetylcholine was produced in the splanchnic region during vagal stimulation and that this substance caused increase in the contraction of the intestinal loop. They presented no evidence as to the exact site of origin of the acetylcholine.

Beznák [37] (1934) observed that the perfusion of the frog's heart with Ringer's solution containing an excess of hydrogen or potassium ions caused the appearance of acetylcholine in the perfusion fluid in concentrations similar to those obtained on vagal stimulation. Vartiainen [38] (1934) reported no evidence of an increase in the amount of acetylcholine or of any similarly acting substance extracted from the frog's heart itself or from the rabbit's auricle as the result of vagal stimulation.

It has been shown by a number of workers that acetylcholine is stable in an acid but not in an alkaline medium, that it is rendered inactive by a blood or tissue esterase and that it is protected from inactivation by physostigmine.

Engelhart and Loewi [39] (1930) and Matthes [40] (1930) conclusively demonstrated the enzymatic nature of this esterase. Stedman, Stedman and Easson [41] (1932) first suggested the term choline esterase for this destructive agent. In 1933 Stedman, Stedman and White [42] confirmed their work of 1932 and further suggested that the choline esterase content of human serum is probably an important factor in controlling the activity of the heart. Ammon [43] (1934) confirmed this work.

36. Bunting, Henry; Meek, W. J., and Maaske, C. A.: The Chemical Transmission of Vagal Effects to the Small Intestine, Am. J. Physiol. **114**:100-105 (Dec.) 1935.

37. Beznák, A. B. L.: On the Mechanism of the Autacoid Function of Parasympathetic Nerves, J. Physiol. **82**:129-153 (Sept. 19) 1934.

38. Vartiainen, A.: Does Vagus Stimulation Cause an Increase in the Acetylcholine Content of the Heart Muscle? J. Physiol. **82**:282-292 (Oct. 17) 1934.

39. Engelhart, E., and Loewi, W.: Fermentative Azetylcholinspaltung im Blut und ihre Hemmung durch Physostigmin, Arch. f. exper. Path. u. Pharmakol. **150**:1-13, 1930.

40. Matthes, K.: The Action of Blood on Acetylcholine, J. Physiol. **70**:338-348 (Dec. 4) 1930.

41. Stedman, Edgar; Stedman, Ellen, and Easson, L. H.: CCXLV. Choline-Esterase: An Enzyme Present in the Blood-Serum of the Horse, Biochem. J. **26**:2056-2066, 1932.

42. Stedman, Edgar; Stedman, Ellen, and White, A. C.: CXXXIX. A Comparison of the Choline-Esterase Activities of the Blood-Sera from Various Species, Biochem. J. **27**:1055-1060, 1933.

43. Ammon, R.: Die fermentative Spaltung des Acetylcholins, Arch. f. d. ges. Physiol. **233**:486-491, 1934.

Stedman and Stedman [44] (1935) further purified this choline esterase and established it as a definite substance.

Kruta [45] (1935) showed that injection of physostigmine makes little difference in the mechanical response to stimulation of a nerve and that it does not alter the onset of fatigue produced by a series of stimuli or by tetany of short duration. However, the response of fatigued muscle is altered by acetylcholine.

In 1933 Dale [46] suggested the term cholinergic to describe the nerve fibers which transmit their action by release of acetylcholine and the term adrenergic for fibers which liberate a substance resembling epinephrine. Dale [47] (1935), in reviewing the work of Langley [48] (1897, 1898 and 1901) and of Langley and Anderson [49] (1902 and 1904) on the regeneration of nerves, concluded, in further support of his chemical terminology, that any cholinergic fiber can functionally replace any other cholinergic fiber and that the same is true of adrenergic fibers but that neither can assume the function of the other.

Dale [47] discussed the changes in pharmacologic conceptions. He expressed the belief that, with the evidence at hand, it can no longer be said that epinephrine and acetylcholine act on their respective nerve endings but that it would be better to say that nerve impulses produce their peripheral effects by liberating these respective substances in relation to the effector cells. "In either case," he stated, "the action of the chemical substance must be on the effector cells, and not on the nerve endings. When atropine or ergotoxine produces its specific

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44. Stedman, Edgar, and Stedman, Ellen: CCCV. The Purification of Choline-Esterase, Biochem. J. **29**:2563-2567 (Nov.) 1935.

45. Kruta, Vladislav: L'acétylcholine produite à l'extrémité des nerfs mateurs est-elle pratiquement efficace pour la contraction musculaire? Arch. internat. de physiol. **41**:187-200 (April) 1935.

46. Dale, H. H.: Progress in Autopharmacology: A Survey of Present Knowledge of the Chemical Regulation of Certain Functions by Natural Constituents of the Tissues, Bull. Johns Hopkins Hosp. **53**:297-347, 1933.

47. Dale, H. H.: Pharmacology and Nerve-Endings, Proc. Roy. Soc. Med. **28**:319-332 (Jan.) 1935.

48. Langley, J. N.: On the Regeneration of Pre-Ganglionic and of Post-Ganglionic Visceral Nerve Fibers, J. Physiol. **22**:215-230 (Nov. 15) 1897; On the Union of Cranial Autonomic (Visceral) Fibres with the Nerve Cells of the Superior Cervical Ganglion, ibid. **23**:240-270 (July 26) 1898; On the Stimulation and Paralysis of Nerve-Cells and of Nerve-Endings, ibid. **27**:224-236 (Oct. 16) 1901.

49. Langley, J. N., and Anderson, H. K.: Observations on the Regeneration of Nerve Fibres, J. Physiol. **29**:iii-v (Dec.) 1902; On the Union of the Fifth Cervical Nerve with the Superior Cervical Ganglion, ibid. **30**:439-442 (Feb. 25) 1904; The Union of Different Kinds of Nerve Fibres, ibid. **31**:365-391 (Aug. 22) 1904; On Autogenetic Regeneration in the Nerves of the Limbs, ibid. **31**:418-491 (Aug. 22) 1904.

paralysis, it does so by rendering the effector cell specifically insensitive to acetylcholine or adrenaline."

The terms myoneural junction and receptive substance, he conjectured, will probably have to be discarded. The question was asked by Dale: "How does the nerve impulse, on reaching the nerve-ending, cause the chemical transmitter of its action to appear? The evidence is meager . . . [but] the latest results (Vartiainen, 1934) support the view that the transmitter is not newly formed by synthesis as each impulse arrives, but is held in some inactivating and protective complex, from which the nerve impulse releases it, and from which it is easily separated by ordinary methods of chemical extraction."

Engelhart and Loewi [39] showed in their investigation in one case that this depot is dependent for its maintenance on the integrity of the nerve endings and that it disappears or becomes depleted when the nerve fibers degenerate.

Recent investigations have tended to indicate that acetylcholine is the chemical transmitter at the ganglionic synapses (Feldberg and Vartiainen,[50] 1934) and that it is the transmitter of the somatic motor nerve impulses to voluntary striated muscle fibers (Dale and Feldberg, 1934, and Lindsley,[51] 1935). Franel's [52] work (1935) did not strongly support the belief that acetylcholine appears after voluntary muscular contractions.

Dikshit [53] (1934) suggested that sensory impulses in fibers of the vagus nerve produce their effects at the central synapse by liberation of acetylcholine. When the vagus nerve was centrally stimulated Feldberg and Schriever [54] found acetylcholine in the cerebrospinal fluid. They refrained, however, from interpreting this finding. Kibjakow's [55] (1933) experiments supported the hypothesis that transmission of impulses from one neuron to another in the autonomic ganglia involves chemical mediation, and Feldberg and Gaddum [56] (1933) suggested that the chemical agent is acetylcholine. Working with cats, Dikshit

50. Feldberg, W., and Vartiainen, A.: Further Observations on the Physiology and Pharmacology of a Sympathetic Ganglion, J. Physiol. **83**:103-128 (Dec. 14) 1934.

51. Lindsley, D. B.: Myographic and Electromyographic Studies of Myasthenia Gravis, Brain **58**:470-482 (Dec.) 1935.

52. Franel, Louise: L'acétylcholine dans le sang, chez l'animal à l'état de repos et de travail musculaire, Arch. internat. de physiol. **41**:256-280 (June) 1935.

53. Dikshit, B. B.: Action of Acetylcholine on the Brain and Its Occurrence Therein, J. Physiol. **80**:409-421 (Dec. 30) 1934.

54. Feldberg, W., and Schriever, cited by Dale.[47]

55. Kibjakow, A. W.: Ueber humorale Uebertragung der Erregung von einem Neuron auf das andere, Arch. f. d. ges. Physiol. **232**:432-433, 1933.

56. Feldberg, W., and Gaddum, J. H.: The Chemical Transmitter at Synapses in a Sympathetic Ganglion, J. Physiol. **80**:xii-xiii (Nov.) 1933.

(1933) found a higher concentration of a substance resembling acetylcholine in the basal ganglia than in the cerebellum or the cortex. Suh, Wang and Lim [57] (1935) injected acetylcholine into the cisterna magna of the dog and observed a rise of blood pressure which was not affected by atropine. In a few animals the respiratory movements were increased.

In April 1935 Armstrong [58] reported an extremely interesting experiment. He attempted to determine whether acetylcholine acts on heart muscle directly or through the mediation of postganglionic vagal fibers. There is ample experimental proof to show that the sympathetic innervation to the heart can be removed but that the cardiac vagal innervation cannot be entirely eliminated. The only vertebrate hearts which have neither sympathetic nor parasympathetic innervation are those of embryos in the early stages of development. Armstrong used the aneural embryonic hearts of Fundulus heteroclitus and Fundulus majalis. He observed that injection of acetylcholine into the heart before the nerves reached it produced no effect. However, after the nerves had reached the auricle the smallest amounts of acetylcholine produced a marked inhibitory effect. He concluded that probably acetylcholine produces its vagal effect by direct stimulation of the vagal postganglionic fibers, which in turn inhibit the heart. Therefore, it was suggested that the vagomimetic substance, recovered from the heart after vagal stimulation, is liberated at the intramyocardial vagal synapses and not at the postganglionic nerve endings.

Cattell and Wolff [59] (1935), generalizing from Armstrong's studies and their work on the action of acetylcholine on the iris of the cat, stated:

> It would appear that the physiological properties of the muscle (adrenergic or cholinergic) are bestowed upon it by the proximity of specific nerve fibers and that, once acquired, the specific sensitiveness is retained, at least for a time, after degeneration of the nerve fibers. Since it is probable that many smooth muscle fibers do not receive direct nerve connections, it is necessary to assume that the nerve has a sphere of influence in functional differentiation which extends beyond its terminations.

COMMENT

A review of this subject illustrates how large and small contributions by many men, widely separated, have helped to round out an important neurobiologic conception. Darwin once said: "Without

57. Suh, T. H.; Wang, C. H., and Lim, R. K. S.: Effect of Intracisternal Injections of Acetylcholine, Proc. Soc. Exper. Biol. & Med. **32**:1410 (June) 1935.

58. Armstrong, P. B.: The Rôle of the Nerves in the Action of Acetylcholine on the Embryonic Heart, J. Physiol. **84**:20-32 (April 26) 1935.

59. Cattell, McKeen, and Wolff, H. G.: On the Site of Action of Acetylcholine and Its Significance, Science **82**:106-107 (Aug. 2) 1935.

speculation there is no good or original observation." One is stimulated to speculate in a subject of this type.

Why is acetylcholine present in the basal ganglia, and why is this region richer in this substance than are the cerebellum and the cortex? What have drugs of the atropine group to do with parkinsonian rigidity? Why does such a rigidity sometimes, but only temporarily, vanish on awakening from sleep or during somnambulism? How do ephedrine and benzedrine, which are so closely related to epinephrine and sympathin, act in narcolepsy and cataplexy? Ephedrine, physostigmine and the potassium salts are startling not only by the specificity of their effects in myasthenia gravis but by the promptness of their action.

Then, one wonders if certain types of tachycardia and bradycardia depend on the choline esterase content of the blood. When acetylcholine is used in emptying the bladder, I wonder if the addition of physostigmine might not make the action more efficacious?

However, the deeper secrets of the propagation of the nerve impulse remain to be uncovered. These newer neurophysiologic conceptions can also be applied in fields of medicine outside the more restricted scope of clinical neurology.

SUMMARY

It has been shown definitely that so-called sympathin, a compound related to epinephrine, exists in two forms: sympathin E, given off by smooth muscle which contracts on sympathetic stimulation, and sympathin I, given off by smooth muscle which is inhibited or relaxed on sympathetic stimulation. It has been shown that these substances may enter the blood stream and thereby produce similar effects on smooth muscle elsewhere than where the original contraction took place. Peripheral parasympathetic effects are transmitted by the liberation of a substance resembling acetylcholine which is rapidly destroyed in circulating blood by an esterase; this destruction can be prevented by the use of physostigmine. The choline esterase is of an enzymatic nature and has been established as a specific destructive agent for acetylcholine. Unconfirmed evidence intimates that stimulation of nerves to voluntary striated muscle fibers produces acetylcholine. There is also evidence that acetylcholine is liberated at ganglionic synapses. Substantive evidence indicates that the chemical receptive action is attributable to the type of nerve fiber that supplies it.

Abstracts from Current Literature

Psychiatry and Psychopathology

PSYCHOSES OF MYXEDEMA. LOUIS J. KARNOSH and RICHARD E. STOUT, Am. J. Psychiat. **91**:1263 (May) 1935.

Thyroid deficiency brings into relief the latent hereditary and constitutional predispositions of the basic personality; since these factors vary considerably, the forms of psychosis associated with myxedema do not conform to any specific pattern. There is no relationship between the metabolic rate and the intensity of the psychosis. In schizoid patients myxedema may precipitate a psychosis which often persists in spite of improvement in the thyroid condition. In cases of cerebral arteriosclerosis and involutional melancholia, mental improvement often follows treatment with thyroid. The importance of adequate thyroid therapy in all cases of myxedema is stressed, and the frequent hopefulness of the outlook is pointed out.

DAVIDSON, Newark, N. J.

THE MENTAL ABILITY OF DELINQUENT BOYS. HOWARD A. LANE and PAUL A. WITTY, J. Juvenile Research **19**:1 (Jan.) 1935.

In 1914 Goddard proclaimed that at least 50 per cent of all criminals are mentally defective. Scrutiny of the methods used in the early studies shows that generalizations of this nature were premature and hyperbolic. The results of mental tests administered to about 700 delinquent children in the St. Charles (Ill.) School for Boys are analyzed. The intelligence of more than 80 per cent of these delinquent boys was below the average for unselected children studied by Terman, and 10 per cent were feebleminded. Recidivists are frequently alleged to be duller than children who are serving a first term in a state school. This was not found to be the case in this study. The group of boys who committed burglary included the largest number of bright children, while the groups of "truant and runaway" boys contained no bright child. The intelligence quotient appears to be unrelated to the extent or the seriousness of the delinquent behavior. Lane and Witty believe, however, that their search for factors associated with the intelligence of delinquent children has been rather unsuccessful. They cannot point to a single item which seems significantly related to the results of the intelligence tests. However, they demonstrated the falsity of many assertions regarding the rôle which intelligence assumes in the behavior and lives of delinquent children.

FERGUSON, Niagara Falls, N. Y.

VOCATIONAL EXPERIENCE AND INTERESTS OF DELINQUENT BOYS. GEORGE E. HILL, J. Juvenile Research **19**:27 (Jan.) 1935.

Nearly 3,000 young men are residents in the Illinois State Reformatory at Pontiac, Ill. To what degree can their failures to make satisfactory social adjustment be attributed to unsatisfactory vocational adjustments? To answer this question, Hill selected for study 1,500 offenders who were sentenced to this reformatory between June 1930 and January 1932. They were from 16 to 26 years of age, the average being slightly over 19 years. Most of them were committed for acquisitive offenses—robbery, burglary and larceny. As measured by the army alpha test they were of average intelligence. Except for 1 per cent who were still in school when apprehended and sentenced, all had been employed at some time, yet nearly three-fourths were unemployed at the time of committing the offenses. Usually the unemployed offender was younger than the employed offenders, had had a more extended career of delinquency and was superior in intelligence and school attain-

ment. He had left school earlier than the employed offender and tended to commit more offenses involving the acquisition of property. The employed offenders were more guilty of sex offenses and assault. The typical young offender had shifted rather frequently from one job to another and had not received satisfactory pay. He had held several jobs before commitment, staying on each job on the average of one year. The boys of this class needed guidance badly, and their vocational adjustments were none too satisfactory. About 60 per cent left school to go to work, usually as soon as possible. Many had serious difficulties with their school work. The vocational aspirations appeared to have been cast higher than the vocational experience. It is obvious that the causes of delinquency are various and complex, and it would be erroneous to conclude that either unemployment or vocational dissatisfaction is the sole motivation for delinquency. Undoubtedly, these factors have operated in actuating young men to commit offenses involving the stealing of valuable property. In Hill's opinion, the problem of proper vocational adjustment is to no small degree a problem of the school. In view of the fact that over half of these boys left school while still of compulsory school age, the school either could have made education more attractive or could have shouldered part of the responsibility for helping the boy start and continue as a successful worker. Hill is of the opinion that a more intensive program of vocational guidance in the schools, with definite vocational training, would do much to prevent delinquency among boys. FERGUSON, Niagara Falls, N. Y.

THE SENSORY ACUITY OF PSYCHOPATHIC INDIVIDUALS. MARION BARTLETT, Psychiatric Quart. **9**:422 (July) 1935.

It is popularly believed by both the laity and the medical profession that persons with neurosis are hypersensitive to sensory impressions. To test this, Bartlett studied the auditory thresholds of twenty-four patients with psychoneurosis, twenty-six with schizophrenia and an unspecified number of normal persons used as controls. An audio-oscillator was used, and twenty readings were taken. The results were expressed in decibels. The average threshold was 53.5 for normal persons, 53.2 for the patients with neurosis and 54.4 for the group of patients with dementia praecox. The range was from 37 to 69 for the group of controls, from 37 to 70 for the patients with psychoneurosis and from 38 to 70 for the patients with schizophrenia. It thus appears that the sensory acuity for the three groups was substantially the same. The apparent hyperacuity of the person with neurosis seems to be based on a deficiency in ability to sustain attention, so that these persons are constantly distracted by trivial stimuli. The apparent impairment of sensory processes in the person with schizophrenia is probably at the complex perceptual level of synthesis of impressions rather than at the simple level of direct sensory perception. DAVIDSON, Newark, N. J.

CLAUSTROPHOBIA. BERTRAM D. LEWIN, Psychoanalyt. Quart. **4**:227, 1935.

Claustrophobia, a form of anxiety hysteria, is a morbid dread of being caught or crushed by a gradual closing in of the space about one. It represents the conscious dread of a wish to return to the uterus, but the question of the specific anxiety has not so far been answered adequately. Lewin analyzes the anxiety associated with claustrophobia. The analysis of two attacks in the case reported led to the conclusion that the patient imagined herself a fetus in the maternal body, but this idea did not cause anxiety. Anxiety arose when the penis entered and threatened to touch her. The intra-uterine fantasy was one of defense or relief from anxiety which arose from the idea of being disturbed or dislodged by the father or his penis. Another anxiety situation arose when the intra-uterine fantasy was interrupted by the fantasy of being born. The process which initiates the fantasy of being in the mother's body is that of partial identification through oral incorporation and is preceded by active oral aggression; that is, it is a latent wish to bite or destroy a sibling fetus by an oral attack. In some instances,

the checking of the oral sadistic wish leads to reversal into its opposite, that is, a wish to be eaten by the mother, with the same consequences. After being ingested the wisher finds himself in the mother's body in place of the fetus. Thus the central fantasy of claustrophobia is the fear of being expelled from the mother's body by the crushing, flushing or other activity of the father. The antecedent of the fantasy is an oral aggression against a real fetus, leading to a partial incorporation and identification with the fetus.

PEARSON, Philadelphia.

THE PROBLEM OF PSYCHOANALYTIC TECHNIQUE. FRANZ ALEXANDER, Psychoanalyt. Quart. **4**:588 (Oct.) 1935.

Since Freud's series of papers on psychoanalytic technic (from 1912 to 1914), various analysts have tried to improve or modify his general principles, without really making any important contribution. Analytic therapy is cumbersome and consumes time and energy, and its outcome is hard to predict in the individual case; so there is an obvious reason for this constant urge toward improvement.

The aim of therapy can be defined as the extension of conscious content over instinctual forces which are isolated from the conscious ego's administrative power either as symptoms or as neurotic behavior. To do this, the three therapeutic factors in the analytic process—abreaction, insight and recollection—are necessary. Abreaction without insight is insufficient, for the process of integration by which the repressed tendency becomes an organized part of the ego does not take place without insight. Insight without abreaction is insufficient, for something which is not in the ego cannot be integrated and the emotional reaction is the sign that the tendency is becoming known to the ego.

Recollection is an indispensable precondition for a repressed tendency to be thoroughly integrated into the ego system, for recollection connects the present with the past. Although the direct therapeutic value of recollection may be questioned, the removal of infantile amnesia must be considered as a unique indication of the successful solving of a repression.

As already stated, innovations in analytic technic have overemphasized the importance of one of these processes. There have been three innovations in technic: (1) neocathartic experiments; (2) reconstruction and insight therapy, and (3) analysis of resistance.

Certain analytic processes overstressed the importance of an intellectual reconstruction of the infantile history. Ferenczi and Rank reacted against this by overemphasizing the importance of abreaction, i. e., by provoking transference reactions and interpreting them in connection with the actual life situation. This abbreviated the length of treatment but neglected the ego's integrating function and the technical device of "working through." Failure with the device of an artificial termination of the analysis caused Ferenczi to dismiss it from his technic and to try creating artificial emotional tensions, first by his active therapy and second by his relaxation therapy. In all of these methods there was regression to cathartic hypnosis and neglect of the intellectual integrating side of therapy —"the working through."

Reich's resistance and layer analysis lays emphasis on hidden forms of resistance; he believes the interpretations should concern themselves with the resistance rather than with the content. This is an artificial and schematic distinction, for the repressing tendencies and the repressed content are connected closely. Similarly, Reich's concept of layer analysis is the result of a tendency to overschematize. It is true that unconscious material may appear in layers and that during development the emotional reactions follow each other in sequence, but they exist in the unconscious not in layers but side by side, and in treatment they do not repeat their chronological order.

Kaiser's resistance analysis is the most extreme distortion of analytic technic on the basis of the primacy of the interpretation of resistance over that of content. Such an analysis is reduced to the sterile procedure of pointing out to the patient

his resistance manifestations. Kaiser loses the reassuring effect of the verbalization of preconscious material with its elimination of the infantile fear of the condemning parents and of the harsh superego.

The process of cure in analysis is the construction of two fundamental psychologic processes: (1) the inviting of unconscious material into consciousness, i. e., emotional experiences—abreaction—and (2) the assimilation of this material by the conscious ego, i. e., insight, synthesis and integration. It is obvious that all technical innovations have been concerned with the first phase of treatment.

As the unconscious consists of psychologic units expressing primitive and infantile connections between instinctual needs and external observations—the units not being harmonized with each other and the external observations not corresponding to the external conditions of the adult—the process of cure must consist in the establishment of new adjustments between instinctual needs and adult external reality through the mediation of the ego.

Therefore, the main function of psychoanalytic interpretations consists in the breaking up of the old overgeneralized and primitive connections and in establishing new connections. Every correct interpretation serves two purposes: mobilization of unconscious material and its integration into the system of consciousness. The integrating process can be accelerated by total interpretation, i. e., interpretation which connects the actual life situation with past experience and with the transference situation. This requires a precise understanding in detail of what is going on in the patient at every moment.

PEARSON, Philadelphia.

COMPLICATED HYSTERICAL AMAUROSIS. C. CHARLIN, Ann. d'ocul. **172**:293 (April) 1935.

The diagnosis of hysterical amaurosis is easily made; sudden blindness occurring when the patient is in the best of health leaves little doubt. The absence of abnormal findings on ocular examination and the presence of stigmas in a neurotic patient confirm this hypothesis.

Charlin reports five cases of hysterical amaurosis. In each case there was an interval between the onset of the actual disease and the appearance of amaurosis, just as in simple hysterical blindness there is an interval between traumatism or psychic shock and the appearance of the visual defect. This interval suggests the possibility of associated neurosis in addition to the primary exciting factor. Stigmas of hysteria must be sought. The diagnosis of hysteria is more natural than that of the rare affection of cerebral blindness which the neurosis simulates. True cerebral blindness is always accompanied by other cerebral symptoms, such as aphasia, hemiplegia and serious psychic disturbances, which necessarily exist in a lesion of the hemisphere sufficiently large to involve the two visual centers.

BERENS, New York.

PSYCHIC COMPULSION PHENOMENA IN PATIENTS WITH DISEASE OF THE BRAIN AND THEIR SIGNIFICANCE FOR THE STUDY OF THE COMPULSION NEUROSIS. ERWIN STENGEL, Jahrb. f. Psychiat. u. Neurol. **52**:236, 1935.

Stengel points out that encephalitis and its sequelae have opened up many new fields for psychopathologic investigation. A study of this disease reveals that patients with organic disease of the brain may present certain phenomena which have hitherto been investigated only psychologically. Some observers, especially those who are oriented neurologically, have even claimed that the occurrence of these phenomena in association with encephalitis has refuted the psychologic theories of neurosis and that the only approach to their understanding will be through cerebral pathology. On the other hand, investigators like von Economo and his school believe that the occurrence of neurotic manifestations in persons with postencephalitis need not necessarily be regarded as definite proof that the neuroses are genetically only organic in nature.

The psychic compulsion phenomena observed in organic disease of the brain are of a more primitive nature; i. e., they are more somatic and less complex in structure than those observed in the compulsion neurosis. Patients suffering from encephalitis and compulsion phenomena fall into two groups: (1) patients with or without parkinsonism in association with which a compulsion neurosis develops and (2) patients in whom psychic compulsion phenomena develop exclusively or predominatingly during an oculogyric crisis. Of these two groups the second is the more common. In the patients of the first group the disease of the brain acts merely as a provocative agent in the development of a latent compulsion neurosis. This does not apply to the patients in the second group, because in most persons with postencephalitis with oculogyric crises there appear sooner or later either fully developed or, at least, indications of compulsive phenomena.

The motor phenomena in cases of parkinsonism bear a striking resemblance to the psychic phenomena associated with the compulsion neurosis. The ambivalence of the compulsion neurosis represents a psychic reproduction of parkinsonian rigidity in which agonists and antagonists act as brakes to each other, with resulting impoverishment of the activity of both, producing the akinesia of parkinsonism. This is analogous to the chief symptom in the compulsion neurosis described by Friedmann, namely, inability to reach final conclusions in the process of thinking and to complete an initiated act. Wexberg believed that clinically the fundamental disturbance in the compulsion neurosis is the inadequacy of motor function from the point of view of time. This belief is based on Freud's conception of the compulsion to repetition as one of the manifestations in the compulsion neurosis.

According to Stengel, psychoanalysis has made a definite declaration as to the instinctual life of the patient with compulsion neurosis which applies also to patients with disease of the brain manifesting compulsive phenomena. In the instinctual life the ego "sees to it" that only the impulses reach the "executive" organ—the musculature—which are permitted to do so by the superego. This is true of the sexual instinct as well as of the destructive instincts. These manifestations are expressed by the musculature regardless of whether they are released by an organic lesion of the brain. With this in mind, one may say that parkinsonism, as well as some other diseases of the basal ganglia, is associated with instinctual manifestations which are included ordinarily in the death instinct. No better example of the craving for absolute rest, which, according to Freud, is the goal of the death instinct, can be furnished than the impoverished motility of an akinetic patient with parkinsonism. This craving for absolute rest has its analog in the stupor of catatonia and melancholia—a symptom which has led to the construction of the hypothesis of the death instinct.

Another manifestation of the death instinct observed in some patients with organic disease of the brain is the compulsion to repetition. Goldstein was the first to recognize the significance of this conception for cerebral pathology. One may say, therefore, that disease of the brain is capable of releasing the inhibition of the compulsion to repetition but that this release may also be accomplished by purely psychic processes of the type frequently observed in tic.

Other manifestations of the destructive instinct of the type observed in parkinsonism are the various seizures which are related to epilepsy. These manifestations were designated by Kleist as "distress phenomena," during which the patient reacts to the instinct for self-destruction and self-mutilation and after which he experiences great relief. Of great interest in this connection is the oculogyric crisis in postencephalitic states. The relation of this crisis to the epileptiform seizure was pointed out by Ewald. Both are followed by sleep, and both can be checked by small doses of hypnotics—doses so small that they are unlikely to produce sleep. Freud included these phenomena in the domain of the destructive instinct, and Stengel regards them as a release of the same instinct.

Various psychic compulsion phenomena are observed during oculogyric crises. The latter are much more adapted to the study of compulsion phenomena than are epileptiform seizures, most of which are usually accompanied by disturbances of consciousness and followed by amnesia. In the course of his investigation of

several cases of oculogyric crisis, Stengel found in many instances a frequent tendency to sadism directed to the patient himself as well as to others. In many patients there appeared, in addition to anxiety and compulsive thinking, a definite state of depression the psychic content of which was typical of that usually observed in melancholia, and during the return to the patient's usual emotional state there occurred a hypomanic phase.

The significance of these observations is interpreted by Stengel as follows. Compulsion neurosis is characterized psychoanalytically by regression to the stage of the development of the infantile instincts in which sadistic tendencies are in the foreground. The sadistic content of compulsive thinking was found with striking frequency in cases of oculogyric crisis in which there was no question as to the organic basis of the disease.

Stengel could find no evidence of anal eroticism in subjects with parkinsonism associated with compulsive thinking, but in the absence of such data as can be obtained only by a thorough analysis no final opinion can be expressed as to this phase of the problem. In many patients with parkinsonism the appearance of the destructive instinct is undoubtedly associated with regression of sexual instincts —not only of those related to the genital organs but of all perverse tendencies. In many of these cases the libido is not infrequently extinguished. An investigation of the reported cases of immoral behavior of patients with disease of the brain reveals that they suffer not from overdevelopment of the sexual instinct in the narrow sense but from aggressiveness, i. e., the destructive tendency, in the psychologic sense. Perversion, however, seems to be unusually rare in such patients.

In this connection Stengel cites Dattner, who recently reported two cases of basophilic cell adenoma of the hypophysis in which the patients had a depressive state resembling melancholia associated with compulsive ideas. These two patients also showed diminution of the sexual instincts and psychic compulsive phenomena in which a displacement could be assumed in favor of the destructive tendencies, even though the latter could not be elicited in the content of the compulsive ideas.

From the point of view of cerebral pathology it is important to bear in mind that psychic compulsive phenomena have thus far been observed in cases in which it must be assumed that the disease affected the deeper parts of the brain, i. e., in locations which have a special significance for the discharge of instinctual processes. The regularity of this occurrence shows unequivocally that there is a relationship between compulsive phenomena and instinctual processes.

Epileptic seizures, as well as oculogyric crises, tend to produce sleep. Some patients subject to oculogyric crises state that they feel sleepy throughout the entire crisis. The restitution of the ego with sleep after the severe disturbances of consciousness during an epileptic seizure, as well as after the slight disturbances of consciousness during an oculogyric crisis, is noteworthy, for in the freudian sense the withdrawal to sleep represents neutralization of the destructive instincts. This interpretation of sleep assumes considerable significance when one bears in mind that in a disease in which the somatic sleep mechanism is as severely affected as in epidemic encephalitis the destructive instinct must play a prominent rôle.

According to Stengel, the oculogyric crisis, unlike any other condition, illustrates what effect motor processes may exert on the content of some psychic processes. This theory as to the nature of the psychic processes in patients with oculogyric crises also confirms the validity of the James-Lange affect theory, which, as is well known, assumes that psychic processes are the fundamental basis of the affects. Of similar significance are the vegetative phenomena and the disturbances of vestibular function observed during oculogyric crises. It is also interesting to note that the disturbances of the muscular apparatus of the eye in patients with postencephalitis are regularly associated with profound changes in the psychic life.

Stengel believes that the oculogyric crisis represents a distorted phase of the motor discharges occurring during the process of falling asleep and that in this sense it is to be regarded as a dissociation of the various components of sleep. The psychic processes during an oculogyric crisis also show a definite relationship between psychic phenomena of sleep, on the one hand, and disease of the vestibular apparatus, on the other.

Stengel is of the opinion that it would be stimulating to direct this type of investigation to the relationship between thinking while falling asleep and the thinking of a patient with schizophrenia, for an understanding of the psychic processes occurring during an oculogyric crisis may shed light on the nature of the motor phenomena observed in subjects with psychoses. It seems to him that the oculogyric crisis represents an extreme phase of a motor act which the patient is unable to execute completely and that in this sense it may be said to be an expression of the organic picture of a psychic compulsion phenomenon.

KESCHNER, New York.

Meninges and Blood Vessels

SUPPURATION OF THE PETROUS PYRAMID. I. FRIESNER, J. G. DRUSS, H. ROSENWASSER and S. ROSEN, Arch. Otolaryng. **22**:659 (Dec.) 1935.

This is an exhaustive review of petrositis. The report is based almost entirely on cases of the acute form. Involvement of the sixth nerve is not a constant sign of deep-seated inflammation of the petrous pyramid. An abscess of the pyramid may exist, and extensive suppuration of the bone may be present without involvement of the abducens nerve. Since paralysis of the sixth nerve exists in cases of simple otitis and may not occur in connection with extensive suppuration, no conclusions as to diagnosis or therapy can be made solely on the basis of the presence or absence of paralysis of the abducens nerve.

The presence of pain in the distribution of the trigeminal nerve in cases of petrositis has been discussed by many men since von Tröltsch mentioned it in 1869 in the report of a case of chronic suppuration of the middle ear. The gasserian ganglion is involved by suppuration of the petrous pyramid. The reason for especial involvement of the ophthalmic branch is not clear. Stretching of the ophthalmic nerve due to its adhesion to the dura, irritation of the great superficial petrosal nerve in its passage through the pyramid, involvement of the sphenopalatine ganglion due to associated sphenoiditis in conjunction with petrositis, suppurative sphenoiditis and osteitis have all been advanced as explanations for the orbital pain. Reports are cited in which the gasserian ganglion was observed to be affected on histologic study in cases of petrositis in which there was no pain. In the five cases in the authors' series paralysis of the external rectus muscle followed a period of pain. "In the consideration of the symptomatology of disease of the petrous pyramid, it is obvious from our material that there are no symptoms which are invariably associated with this condition. The most significant symptom is pain," the presence of which is more important than its location. The later the onset of pain the graver is its significance. In the present cases cessation of pain indicated beginning of recovery. "We therefore have found little ground for the belief that the cessation of pain is a grave symptom and is indicative of the extension of the suppurative disease beyond the limits of the bone." External rectus palsy appearing late in the disease is of much greater significance than that occurring early.

In numerous reports of roentgenographic findings from the literature cases are described in which the petrous apex was involved, with recovery following paracentesis or simple mastoidectomy. Also cases of involvement of the fifth and sixth nerves with roentgenographic evidence of petrositis have been reported in the literature, with recovery following simple mastoidectomy. The authors conclude that roentgenographic evidence alone does not constitute an indication for surgical intervention.

They point out that extensive petrositis has been noted histologically in patients who died of intracranial complications of otitis with no clinical signs of petrositis even in retrospect. They observed a number of cases of intracranial involvement in which the apex of the petrous bone was mildly involved or was not affected. They believe that from a pathologic standpoint the process is a combination of osteitis and osteomyelitis. An analysis of the pathway of infection in the present

cases shows that the posterosuperior route was most frequent. They again emphasize that all lesions of the petrous pyramid do not extend to the apex, and when the apex is involved the pathologic changes are usually not so marked as in the lateral portion of the pyramid. They observed that the "greatest expression of the disease process [is] in the petrous pyramid between the superior semicircular canal and the external auditory meatus. Furthermore, in fourteen of the twenty-four cases the lesion was most manifest at the superoposterior margin of the petrosa." They make the point that the apex may be involved in cases in which the duration of the disease is longest.

In fifteen cases definite involvement of the gasserian ganglion was shown by swelling and degenerative changes of the cells and inflammatory exudate within the cells, the nerve and the adjacent portion of the dura. Inflammatory changes in the gasserian ganglion could not always be correlated with the clinical symptoms or the distribution of pain, which was absent in some cases and present in others, nor could the authors account for the presence or absence of symptoms.

Labyrinthitis may be independent of petrositis or secondary to it. In some cases in which labyrinthine symptoms were present no labyrinthitis was observed histologically. The dura walls off the disease, as evidenced by thickening and scar formation. As a result of scar formation in the bone the dura may be drawn through the defect in the cortex into the petrous pyramid and in this way may wall off the disease process.

Fever is not characteristic of suppuration of the petrous pyramid. In most of the authors' cases the temperature varied from 99 to 100 F. Although the pathologic material showed frequent involvement of the seventh nerve, facial paralysis was infrequent. The eighth nerve is not frequently involved in the labyrinth. It may be involved either in the labyrinth or in the internal canal. In rare instances the ninth and tenth nerves are involved by invasion of the peribulbar region, causing hoarseness and difficulty in deglutition. In two of the present cases pathologic lesions were noted, with no clinical symptoms.

The authors believe that in many cases suppuration confined within the petrous pyramid results in spontaneous cure and therefore does not call for immediate operation. It is pointed out that operation in cases reported early in the literature was performed to provide drainage when there was evidence of extension beyond the limits of the bone.

Extradural abscess has been observed frequently above the internal auditory canal and not at the apex.

"We have learned from our pathologic material that in the vast majority of cases suppuration of the pyramid extended from the middle ear and mastoid antrum through the superior and posterior group of perilabyrinthine cells. . . . In only a few was the major expression of disease at the apex of the pyramid. As has been stated before, in all the cases observed clinically the patients have recovered with normal ears and normal hearing. Of all the types of surgical intervention described in the literature we have utilized a procedure described by Eagleton and have added few modifications. . . . We have not found it necessary to perform radical mastoidectomy." The authors have never found it necessary to perform radical mastoidectomy in cases of the acute condition.

HUNTER, Philadelphia.

CHRONIC COCCIDIOIDAL MENINGITIS. K. H. ABBOTT and O. I. CUTLER, Arch. Path. **21**:320 (March) 1936.

Coccidioidal granuloma usually begins as a focal lesion in the skin or lungs. In many cases the infection ultimately becomes generalized, and metastases may be observed in various organs or tissues, including the central nervous system and its coverings. In other cases the lesions are widespread and systemic; in these the original focus is not discoverable. In this group, in some instances, the nervous system is affected to the apparent exclusion of all other structures. The object in this paper is to review the various cranial and intracranial lesions provoked

by this disease, with particular attention to the form of chronic meningitis which develops without clinical evidence of the original focus of infection. Abbott and Cutler studied a series of 7 cases of this type. In addition, they summarized the observations in 7 other cases in which the cranial and intracranial lesions were secondary to a known distant focus or to systemic infection. These cases were gathered from a series of about 15,000 autopsies.

Leptomeningitis is the most important intracranial lesion caused by coccidioidal granuloma. The meningeal lesion is a chronic inflammatory process which appears in three characteristic forms:

1. Nodules, which are small, round or irregular and frequently flattened and vary in size from that of a millet seed to that of a pinhead. These tend to follow the course of the vessels and are distributed over the dorsolateral surfaces and at the base of the brain. Microscopically the lesions are practically identical with those caused by the tubercle bacillus except that coccidioides are present.

2. Larger, irregular, plaquelike patches of exudate, which occur in the spinal meninges and in the basilar cisterns. These plaques may vary from 0.5 to 2.5 cm. in diameter. They can be distinguished both macroscopically and microscopically from tubercles caused by acid-fast bacilli. These accumulations are composed of both cellular exudate and granulation tissue.

3. Thick accumulations of plastic exudate. These are usually in the basilar cisterns, but it is probable that the exudate may also involve the spinal meninges. The meninges in all three types show more scarring than is usual in tuberculous meningitis.

WINKELMAN, Philadelphia.

REGULATION OF CEREBRAL CIRCULATION. J. TINEL and G. UNGAR, Presse méd. **44**:169 (Jan. 29) 1936.

Although failure of the cerebral blood vessels to react to the usual vasoconstrictor substances (such as epinephrine) is commonly supposed to be due to the absence of intracranial vasomotor sympathetic nerves, the condition can also be explained by a contrary hypothesis, i. e., by the existence of a sympathetic plexus so sensitive as to compensate promptly for any vasomotor change. Tinel and Ungar cite four sets of facts to support the latter contention. Among lower mammals, such as rabbits, the young animals have definite cerebral sympathetic nervi vasorum. Such nerves cannot be detected in older animals. Man needs this regulation, and it is unlikely that so useful a structure is lost in the course of evolution. Sympathetic fibers accompanying cerebral vessels have been observed by Hassin (The Nerve Supply of the Cerebral Blood Vessels, ARCH. NEUROL. & PSYCHIAT. **22**:375 [Aug.] 1929) and Penfield (Intracerebral Vascular Nerves, ARCH. NEUROL. & PSYCHIAT. **27**:30 [Jan.] 1932). Clinically, the existence of angiospasm, transient hemianopia associated with migraine and intermittent aphasia can best be explained on the basis of an intracranial vasomotor sympathetic system. Experimental proof is also cited by Tinel and Ungar to show that epinephrine causes cerebral vasoconstriction if the superior cervical ganglion is removed or if the patient is previously treated with ergotamine tartrate—processes which paralyze the inhibitory mechanism, allowing a previously masked sensitiveness to vasoconstrictor substances to appear. It is necessary for the brain to be protected against sudden changes in vascular caliber, and to effect this a highly complex and sensitive system of intracranial sympathetic innervation is essential.

DAVIDSON, Newark, N. J.

Diseases of the Brain

XANTHOMATOSIS AND THE SYNDROME OF DIABETIC EXOPHTHALMIC DYSOSTOSIS. S. BERNARD WORTIS, ABNER WOLF and CORNELIUS G. DYKE, Am. J. Dis. Child. **51**:353 (Feb.) 1936.

Wortis, Wolf and Dyke report three cases. The first was that of a boy aged 2, with roentgenographic evidence of xanthomatosis, particularly in a large area in the parietal region; operation was performed, and the patient died; no autopsy

was done. The second case was that of a boy aged 3, who had manifested symptoms from the age of 2 years and presented exophthalmos, polydipsia, polyuria and a slight swelling in the region of the left temporomandibular joint; the condition was diagnosed clinically and roentgenologically as xanthomatosis of the Hand-Schüller-Christian type; this child was given roentgen radiation and hypodermic injections of pitressin, with considerable improvement. The third case was that of a boy aged 10, who had a small swelling over the occipital region; a roentgenographic diagnosis of xanthomatosis was made; diabetes insipidus and exophthalmos were absent; roentgen irradiation was given, with improvement as shown by roentgenographic examination. The authors assume that roentgen irradiation is of considerable aid in the treatment of the skeletal structures involved.

WAGGONER, Ann Arbor, Mich.

PUNCH-DRUNK. EDWARD J. CARROLL, Am. J. M. Sc. **191**:706 (May), 1936.

Carroll delineates the clinical syndrome of "punch drunkenness" by describing a typical composite case, which he assembled from laymen whose business was a keen study of boxers and from incomplete observation for two years in many cases of punch drunkenness. In the course of the condition in a typical case the tolerance to all blows to the head becomes reduced. After a blow on the head the legs become shaky and numb. The coordinating ability diminishes, as shown in the poorer defensive tactics. Deterioration in attention, concentration and memory develop, and the punch-drunk person may come to resemble some one who is "just a little drunk." Punch drunkenness is a self-limited rather than a progressive form of encephalopathy. In severe forms disturbances in speech, unsteadiness in gait and mental and personality changes become more marked. Such patients have no insight into their condition. It is usually the fighter of the wide-open slugging type, much more than the clever boxer, who relies on speed and coordination in whom this syndrome is likely to develop. It is estimated that about 5 per cent of men who remain in the ranks of professional boxers for five years or more become definitely punch drunk. The prominence of objective mental changes and the freedom from symptoms are in contrast to the many subjective complaints in the postconcussion syndrome. Of two encephalograms, one showed no demonstrable changes; the other revealed definite cortical atrophy, which was localized in the left frontal region. It is postulated that the underlying pathologic change consists of small, discrete vascular lesions.

MICHAELS, Boston.

SYNDROME OF MENINGEAL FIBROBLASTOMA ARISING FROM LESSER WING OF SPHENOID BONE. ROBERT A. GROFF, Arch. Ophth. **15**:163 (Feb.) 1936.

In 1934 Alpers and Groff presented a definite clinical picture in patients with meningeal fibroblastoma arising from the lesser wing of the sphenoid bone. Five additional cases are reported, and all nine cases are discussed in order to clarify the syndrome. As originally stated, this syndrome consists of primary atrophy of the optic nerve or the Kennedy syndrome, defects in the visual fields, which usually take the form of complete homonymous hemianopia and sometimes of quadrantic hemianopia, paralysis of the third nerve and unilateral impairment of the olfactory nerve. Unilateral exophthalmos is present in some cases. Additional symptoms are motor paralysis, impairment of memory and disturbances of the pituitary body, with minor changes in the sella turcica—"top normal" size, slight erosion of the dorsum and of the anterior clinoid processes and, in some instances, unilateral deformity of the sella turcica.

Paralysis of the oculomotor nerve was observed in three instances and of the abducens nerve in one instance. The trochlear nerve was not involved in any case. In two cases there were both subjective and objective disturbances of the first and second divisions of the fifth nerve. Unilateral impairment of the branch to the levator palpebrae muscle was recorded in two instances. Objective sensory disturbances were not observed in any of the nine instances. In one patient signs

of motor weakness were manifested by paresis of the arm and face, with increased reflexes. In another there was subjective weakness in the lower part of both legs. In both instances these sensations disappeared after operation. Disturbances of the pituitary gland were manifested in two patients by loss of libido, questionable menstrual disturbances and a gain in weight, and in another patient, by loss of libido, polyuria, a gain in weight and cutaneous changes. Uncinate fits, unilateral disturbance of taste and impairment of memory occurred in one patient each.

The roentgenographic findings were not constant. In one case slight erosion of the posterior clinoid processes was shown; in another, thickening of the anterior clinoid processes; in a third, rarefaction of the dorsum; in a fourth, a thin, curved shadow about the pit of the floor; in a fifth, some atrophy of the dorsum, with pointing of the anterior clinoid processes, and in a sixth, complete erosion of the dorsum sella and posterior clinoid processes, with a thin, depressed floor. In two cases there was hyperostosis of the sphenoid ridge and adjacent bones. Encephalographic studies showed unilateral deformity of the cisterna interpeduncularis on the side of the tumor. In discussing the differential diagnosis of these conditions, Groff outlines four possible considerations: suprasellar tumor, intrasellar tumor with parasellar extension, aneurysm of the internal carotid artery and intra-orbital growth.

SPAETH, Philadelphia.

NEUROFIBROMATOSIS. ALEXANDER MILLER, Arch. Surg. **32**:109 (Jan.) 1936.

A case of neurofibromatosis is reported in which there were, in addition to the typical nerve tumors, cutaneous pigmentation and elephantiasis, kyphoscoliosis with compression myelitis, and sarcomatous degeneration in more than one neurofibroma. The bone changes can be described under four headings: (1) partial atrophy and arrest of growth, (2) local hypertrophy and hyperplasia, (3) local changes of pressure due to growth of adjacent tumors and (4) unexplained osteoporosis or malacia of the long bones and the vertebral column.

Pathologically, the principal lesion in neurofibromatosis is proliferation of the endoneurium, with hyperplastic changes in the perineurium. The process frequently proceeds to a point at which all evidence of nerve fibers is lost. There may be localized thickening of the nerves, palpable as small subcutaneous nodules, or rather diffuse involvement resulting in fusiform strands. The lesions may vary from the small, discrete seedlike tumor to the large, coarse communicating plexiform neuroma. The peripheral nerves are by far the most frequently and extensively involved, but neurofibromatosis of perhaps all the cranial, spinal and sympathetic nerves has been described. In their order of frequency, changes have been noted in the ulnar, radial, orbital, gluteal, sciatic and crural nerves. Pain is usually absent. If present, it is neuralgic or neuritic. The nerves may be tender on pressure. Paralysis or atrophy rarely occurs.

Malignant degeneration may occur in these nodules, but rarely primarily in more than one nodule. The case reported here is of additional interest in that malignant degeneration of various degrees was present in almost all of seven large tumors studied.

GRANT, Philadelphia.

EARLY ASYMPTOMATIC ACOUSTIC TUMOR: REPORT OF SIX CASES. MARY HARDY and S. J. CROWE, Arch. Surg. **32**:292 (Feb.) 1936.

Examination of serial sections of the temporal bones of 250 patients revealed a small tumor of the acoustic nerve in six instances. Each growth was entirely within the internal auditory canal. The largest was about 5 mm. in diameter and the smallest about 0.25 mm. The vestibular nerve was involved by the tumor in four instances and the cochlear nerve in two. Histologically, five of the tumors were alike in cellular structure; they resembled large tumors observed on the acoustic nerve and in the cerebellopontile angle. The sixth tumor was different from any other growth seen in this region. An angiomatous network of blood vessels was present in three cases in which there was a tumor and in

seven in which there was no tumor; the network involved the vestibular nerve. These lesions, both the tumor and the angiomatous network, were asymptomatic. Irritative symptoms are not produced by growths that are too small to cause compression of the contents of the internal auditory canal.

GRANT, Philadelphia.

POST-TRAUMATIC NARCOLEPSY. GEORGE W. HALL and GEORGE B. LEROY, J. A. M. A. **106**:431 (Feb. 8) 1936.

Hall and LeRoy point out that early writers regarded the syndrome of somnolence and cataplexy as a neurosis, while more recent observers believe that actual pathologic changes are present. The majority of cases of posttraumatic narcolepsy have been reported since the war. It is questionable in some cases whether the condition is the sequel of trauma or of encephalitis. Osnato and Giliberti showed how the diffuse parenchymatous degeneration of the brain following injury to the head may closely resemble the lesion of encephalitis, of whatever cause. They also demonstrated a similarity in the symptomatology of the early stages of head injury and the early phases of acute encephalitis and showed statistically the frequency of somnolence in the two conditions. Hall and LeRoy divide cases of narcolepsy into two groups. Group 1 includes those in which diurnal attacks of sleep and cataplexy are presented, as described by Gélineau. The term true narcolepsy is therefore limited to this group. Group 2 includes cases in which pathologic and paroxysmal attacks of somnolence only are presented. In the majority of the cases which the authors discuss the condition is typified by the close relationship between the time of the trauma to the head and the onset of pathologic and paroxysmal attacks of diurnal sleep. The investigation of cases of posttraumatic narcolepsy renews interest in the etiology of the so-called idiopathic types of narcolepsy, for in the cases considered the exciting cause is rather obvious and one can speculate with some degree of certainty on the changes in the brain. At the same time, one cannot ignore the part that epidemic encephalitis or some other inflammatory disease of the hypothalamic region plays as a cause of narcolepsy, as it is an obvious fact, which must not be overlooked, that narcolepsy with cataplexy is rarely the sequel of head injury, which is a rather common accident.

EDITOR'S ABSTRACT.

PONTILE ABSCESS: REPORT OF TWO CASES. B. W. LICHTENSTEIN and HOWARD ZEITLIN, J. A. M. A. **106**:1057 (March 28) 1936.

Lichtenstein and Zeitlin discuss two cases in which the abscess possessed a capsule of young connective tissue and was associated with nonsuppurative encephalitis in its immediate vicinity, mild degenerative changes in the ganglion cells and marked meningitis. The histopathologic changes in the poorly developed capsule surrounding the abscess, with the changes in the adjacent brain tissue and the reactive phenomena in the subarachnoid space, were similar to those previously reported by Kölpin, by Diamond and Bassoe and, particularly, by Hassin. The elements participating in the formation of the capsule were exclusively mesodermal. Although the capsule was immature, its differentiation into three layers was fairly evident. The brain tissue about the wall of the abscess contained numerous blood vessels at a short distance above and below the abscess, their adventitial coats being swollen and thickened and their perivascular spaces (Virchow-Robin) markedly infiltrated with plasma cells. The last-mentioned changes corresponded with those described as nonsuppurative encephalitis. In one case the presence in the subarachnoid space of gitter cells and the catabolic products in connection with the brain abscess was undoubtedly instrumental in producing meningeal reactive phenomena. The experimental work of Weed, Forster and others, as well as the facts derived from a study of pathologic changes in man, conclusively proved that the flow of tissue fluid is from the Virchow-Robin spaces to the subarachnoid spaces of the brain and cord. Passage of gitter cells and waste substances into the subarachnoid space causes a reactive phenomenon in the meninges, which is

known as aseptic meningitis. Concerning the etiology of the abscess in the first case in this series, there are several possibilities, since a detailed history was not available. If the infection of the eye can be considered primary the abscess can be readily explained as a metastatic lesion. On the other hand, conjunctivitis may have developed when the pontile abscess became large enough to involve first the seventh nerve, making it impossible to close the right eye completely, and later the nucleus of the trigeminal nerve on the right side, producing corneal anesthesia. In the second case only contralateral hemiplegia was shown clinically. The clinical picture so much resembled that of a cerebral lesion that the cortex was explored surgically. The location of the abscess in the pons was such that it precluded additional involvement of a cranial nerve, which is essential in the correct diagnosis of a pontile lesion.

PARAPHASIC SIGNS IN DIFFUSE LESIONS OF THE BRAIN. FRANK J. CURRAN and PAUL SCHILDER, J. Nerv. & Ment. Dis. **82**:613 (Dec.) 1935.

From detailed reports on the paraphasic utterances of patients with toxic or traumatic psychosis, Curran and Schilder note certain features of similarity to the disturbance in speech associated with schizophrenia. The material illustrates the need of recognizing that the character of the speech is the result not of a lesion but of the person's total previous experience. Speech as the result of organic lesions becomes more primitive, but the type of mistake that the person with paraphasia makes is due largely to his individual experiences. Nevertheless, the similarity of speech in paraphasia to that in schizophrenia points to the possibility of an organic nucleus for disturbances of speech in schizophrenia.

HART, Greenwich, Conn.

PALATAL PARALYSIS IN EXTRA-FAUCIAL DIPHTHERIA. G. W. RONALDSON and W. HOWLETT KELLEHER, Brit. M. J. **1**:1019 (May 18) 1935.

Palatal paralysis undoubtedly occurs in association with extrafaucial diphtheria, and theories of pathogenesis which postulate a contrary assumption are untenable. In the nonfaucial varieties of diphtheria palatal paresis is less common and tends to occur at a later date than in faucial diphtheria. Paresis of accommodation is the most frequent and usually the earliest paretic sequel of extrafaucial diphtheria.

BECK, Buffalo.

THE PATHOGENESIS OF CATAPLEXY ON ANGER. MAX LEVIN, J. Neurol. & Psychopath. **16**:140 (Oct.) 1935.

In cases of narcolepsy attacks of cataplexy may result from anger. The mechanism involved is different from that of cataplexy provoked by laughter. Anger is accompanied by an aggressive impulse to action, which the patient strives to suppress. Physiologically, the excitation of cerebral areas accompanying such an emotion is opposed by an inhibition, which, if sufficiently strong, may lead to a cataplectic attack. Thus, the cataplexy is an indirect result of anger. In the case of laughter, the emotion is accompanied by an absence of impulse, and the resulting cataplexy is thus the direct result of the emotion.

N. MALAMUD, Ann Arbor, Mich.

ENCEPHALOTRIGEMINAL ANGIOMATOSIS. J. CHARAMIS, Ann. d'ocul. **172**:405 (May) 1935.

Charamis reports a case in which vascular nevi occurred in the right trigeminal region associated with a calcified angioma of the homolateral occipital region.

BERENS, New York.

DELIRIUM OF INTERPRETATION AND MULTIPLE CEREBRAL TUMORS. F. D'HOLLANDER and M. LEROY, J. belge de neurol. et de psychiat. **35**:621 (Nov.) 1935.

D'Hollander and LeRoy describe a case of multiple tumors of the cerebrum associated with interesting mental phenomena. The mental difficulties at first were mainly those of memory, attention and the performance of bizarre acts, which began several months before the evidence of increased intracranial pressure. In addition, there were difficulty in finding the proper word and verbal perseveration. There was no receptive aphasia. The patient was unable to name objects. Autopsy revealed tumors in the frontal and temporal lobes on the left side and the right parietal lobe, all the tumors being hemorrhagic.

WAGGONER, Ann Arbor, Mich.

NEW CASE OF COMPLETE ANOSMIA AND AGEUSIA OF TRAUMATIC ORIGIN. J. HELSMOORTL JR., R. NYSSES and R. THIENPONT, J. belge de neurol. et de psychiat. **35**:656 (Nov.) 1935.

The authors state that real ageusia is rare in posttraumatic conditions. Complete ageusia is usually of central origin and may occur as a unilateral phenomenon associated with certain types of hemiplegia. Also, it has been noted after intracranial section of the fifth nerve and may be associated with diminution of somatic sensation. It may occur also in hysteria. The authors review the theory of the mechanism of gustatory impressions held by Kleist, in which it is stated that such impressions are transmitted by the chorda tympani nerve and the nervus intermedius to the anterior two thirds of the tongue and by the glossopharyngeal and possibly part of the vagus nerve to the posterior part of the tongue. The bulbar center for taste is constituted principally by the dorsolateral nucleus of the glossopharyngeal nerve. The central pathway for taste ascends, after partially crossing in the region of the pons, and ends in the anterolateral nucleus or the median nucleus of the thalamus, near the trigeminal zone. From here the gustatory path proceeds through the posterior part of the internal capsule to the inferior part of the central convolution, where presumably the gustatory center coincides with the subcentral area. It is stated that this localization is confirmed in cases of traumatic lesion. According to other authors the cortical center for taste is in the hippocampal convolution near the uncinate gyrus, associated closely with the olfactory center. It is stated that in true anosmia there persists a partial perception of irritant odors, which suggests that the absence of perception of irritating odors is strongly in favor of a diagnosis of hysteria or malingering. In the cases described pyridine and ether were perceived while chloroform and alcohol were not. This suggested to the authors that the condition was of organic origin.

WAGGONER, Ann Arbor, Mich.

EPILEPSY AND THE TEMPORAL LOBE. K. H. STAUDER, Arch. f. Psychiat. **104**:181 (Oct.) 1935.

Stauder reports clinicopathologic studies on the relationship between epilepsy and syndromes of the temporal lobe. Sixty-eight cases were studied, but Stauder considered that in only fifty-three were the clinical data satisfactory for drawing conclusions. Histologically, definite pathologic signs in the cornu ammonis were shown in thirty-six cases and none in seventeen. In only three of the first group were no symptoms of involvement of the temporal lobe shown, while in fifteen of the second group no such clinical signs of disturbance appeared and in two only questionable signs were shown. In discussing these cases, Stauder analyzes the problem, first, whether in patients with disease of the temporal lobe one finds clinical features of epilepsy and, second, whether in epilepsy one finds clinical symptoms of disease of the temporal lobe.

With regard to the first question, he finds that epileptic convulsions occur in a large number of diseases of the temporal lobe and that when convulsions are not present there are other symptoms which may be regarded as equivalents

of epilepsy. The uncinate fits, the dreamy states of Jackson, the experiences of déjà-vu and narcoleptic spells are all clinical features usually considered as belonging to the wider circle of forms of epilepsy. The mental disturbances which have been described as occurring in disease of the temporal lobe are again closely related to epilepsy. Thus, one frequently observes states of confusion and twilight states, hallucinatory experiences of a religious character, outbursts of temper and deterioration of a type which is frequent in epilepsy. The Korsakoff-like symptoms which are sometimes observed in these diseases are also considered by Stauder to be closely related to epileptic psychosis.

Concerning the second question, Stauder finds that in a large number of patients with epilepsy, symptoms of involvement of the temporal lobe are present. These are mainly manifested in the various forms of aura which precede the epileptic attacks and may thus be regarded as the starting-point of disturbance. Olfactory, gustatory, auditory, vestibular, optic and aphasic forms of aura occur in the majority of cases, and Stauder believes that all these functions are distinctly related to the temporal lobe.

W. Malamud, Iowa City.

Peripheral and Cranial Nerves

Observations on the Etiologic Relationship of Vitamin B (B_1) to Polyneuritis in the Alcoholic Addict. Norman Jolliffe, C. N. Colbert and Philip M. Joffe, Am. J. M. Sc. **191**:515 (April) 1936.

Forty-two subjects were tentatively selected for this study because of their ability to give an adequate and accurate history of the diet with polyneuritis and the alcoholic intake. The diet of twenty-six persons who were addicted to the use of alcohol failed quantitatively and for a sufficient period to contain adequate amounts of vitamin B as compared with the predicted requirement (Cogwill's formula). In eight subjects without polyneuritis but with addiction to alcohol of long duration, the diet contained adequate amounts of vitamin B as compared with the normal requirement. In eight subjects without polyneuritis the diet was deficient in vitamin B intake as judged by the ratio of the vitamin B to the caloric intake with alcohol, the protective factor being the short duration of the alcoholic bout (not over three weeks in six of the eight cases). The time required to produce clinical evidence of polyneuritis on a vitamin B-deficient diet is variable. In a subject having a vitamin B-caloric ratio equivalent to but 30 per cent of the predicted requirement clinical evidence of vitamin B deficiency develops earlier than in a subject having 60 per cent of the predicted requirement. Alcohol per se, even when used in large amounts over a long period, had no direct toxic action on the peripheral nerves. Jolliffe, Colbert and Joffe believe that beriberi and polyneuritis in the person addicted to the use of alcohol are one and the same disease and that both conditions are due to lack of vitamin B. There was no clear correlation between the degree of vitamin B deficiency and the presence or absence of involvement of the central nervous system. To prevent possible polyneuritis, the alcohol addict should consume a full mixed diet, supplemented by about 250 mg. equivalent (50 Sherman or 25 international units) of vitamin B for each hundred calories of alcohol he consumes.

Michaels, Boston.

Operative Exposure of the Facial Canal, with Removal of a Tumor of the Greater Superficial Petrosal Nerve. G. Edward Tremble and Wilder Penfield, Arch. Otolaryng. **23**:573 (May) 1936.

This article is the report of a case of perineurial fibroblastoma arising in the vicinity of the geniculate ganglion, with removal. Tremble and Penfield have found no report of a similar case. The patient had left facial paralysis for five years and tinnitus and partial deafness of the left ear for two and a half years. Otorrhea, otalgia, dizziness, nystagmus, vertigo and difficulty in walking had not been noted. Physical examination gave normal results except for paralysis

of the left side of the face, involving the upper as well as the lower portion, with an occasional involuntary movement of the left angle of the mouth, indicating attempted regeneration of the nerve. Gustatory sense was impaired on the left side anteriorly. The right parotid duct had a much larger papilla than the left. However, it excreted the same amount of saliva as the left. The right submaxillary and sublingual glands excreted 0.61 Gm., as compared with 0.17 Gm. on the left, owing apparently to interruption of the fibers of the chorda tympani. The conclusion was that there was impairment of the fibers of the chorda tympani on the left, as shown by the loss of taste and the decrease of salivary secretion, but not of the fibers supplying taste to the posterior third of the tongue or supplying the parotid gland, both of which are innervated by the ninth cranial nerve. The great superficial petrosal nerve was examined as follows: A quantitative estimation of the lacrimal secretion was made by means of a tampon placed near the external canthus of each eye, without the use of a local anesthetic. The weight of the tampon before and after placement was determined. The secretion of tears was stimulated by means of ammonia, and the difference in the quantity and the normal amount was measured. The right gland secreted 0.055 Gm. in two minutes and the left 0.001 Gm., showing a marked diminution for the left as compared with the right and evidence of involvement of the facial nerve at or proximal to the geniculate ganglion or of involvement of the great superficial petrosal nerve. Hearing in the Weber test was lateralized to the left. Air conduction was greater than bone conduction. There were three exostoses in the left auditory meatus. Hearing for high notes was greatly diminished. Caloric tests indicated impairment on the left side. Radical mastoidectomy was performed, and the facial nerve was exposed from the horizontal canal to the stylomastoid foramen. The stapes below the nerve was carefully avoided. The nerve was traced around the bend, and just above the oval window, 4 mm. from the bend, the neuroma was observed to extend through the bone from the facial canal to the subdural space, apparently following the canal of the great superficial petrosal nerve. The main portion of the tumor thus presented beneath the dura on the anterior aspect of the petrous pyramid. As much of the growth as possible was removed.

HUNTER, Philadelphia.

MULTIPLE PARALYSIS OF THE CRANIAL NERVES DUE TO EXTENSION OF RHINOPHARYNGEAL TUMORS TO THE BASE OF THE SKULL. H. ROGER and J. PAILLAS, Rev. d'oto-neuro-opht. **13**:165 (March) 1935.

Tumors of the pharynx are divided into two classes (Jacod): those that develop at the expense of the vault and those that invade the lateral walls. Tumors of the first class develop in the nasopharyngeal, nasal and sinus cavities and affect only the branches of the cranial nerves, without invading the endocranial cavity except by extension through the sphenoid and ethmoid cavities. Tumors of the second class extend to the cranial base along the peritubal aponeurotic fasciae, through the anterior lacerated foramen; the floor of the middle fossa is penetrated in the zone of the petrosphenoid bone, and the tumor extends under the dura, involving the third, fourth, fifth and sixth cranial nerves. Rarely does it extend over the petrous ridge to the internal auditory meatus and involve the seventh and eighth nerves. Less rarely the extension is toward the median line, involving the posterior lacerated foramen and the hypoglossal canal and causing paralysis of the last four cranial nerves.

Metastatic propagation is by means of blood or lymph vessels or the nerve sheaths. Endocranial metastasis by way of the vessels is unknown; the course of metastases of this type is along the nerve sheaths. Propagation through lymphatic channels reaches the retropharyngeal nodes or the superior ganglia of the internal jugular chain. Metastases to the ganglia in the region of the posterior lacerated foramen affect the ninth, tenth and eleventh nerves and sometimes the twelfth nerve.

In the majority of cases the symptoms begin with headache or facial neuralgia. Headache is usually in the vertex and is not ameliorated by the usual anodynes. Facial neuralgia is often the only early symptom. It occurs in paroxysms, and the three branches of the nerve are successively involved, the ophthalmic branch being affected last. It is accompanied by hypesthesia. In typical cases the triad of symptoms consists of neuralgia, hypo-acousis and homolateral strabismus. Modifications of the cerebrospinal fluid are indefinite or absent, owing to the fact that the dura is rarely penetrated and to spontaneous decompression. When papillary stasis exists it is caused by edema in the pericancerous tissues. The fluid may contain a little albumin and a few cellular elements. Roentgenography is an important aid in the diagnosis, and plates should be made from many angles. It reveals evidence of absorption of bone and sometimes a shadow of the tumor itself. Evolution is progressive and is followed, step by step, by successive paralysis of the cranial nerves. Cachexia develops, and death occurs, usually from bulbar syncope.

The clinical syndromes are composed of certain anomalous forms and the following classic syndromes: (1) syndrome of the petrosphenoid cross-roads, with association of unilateral paralysis of the second, third, fourth, fifth and sixth nerves, facial neuralgia, total unilateral ophthalmoplegia and amaurosis; (2) syndrome of the point of the petrous bone, comprising paralysis of the trigeminal nerve and the external rectus muscle; (3) syndrome of the posterior lacerated foramen, characterized by paralysis of the ninth, tenth and eleventh nerves, "sign of the curtain," absence of taste over the posterior third of the tongue, sensory disturbances of the velopharyngolaryngeal mucosa, a cough like pertussis, modification of the salivary secretion, paralysis of the trapezius and the sternocleidomastoid muscle and hemiparalysis of the velum and larynx; (4) syndrome of the jugulohypoglossal canal, characterized by the syndrome of Vernet, paralysis of the hypoglossal nerve and lingual hemiatrophy, with deviation of the point of the tongue to the normal side while the tongue is in the mouth and to the opposite side when it is protruded, and (5) unilateral paralytic global syndrome of the cranial nerves.

The anomalous forms are: (1) syndromes in which the continuity of the paralytic progression is broken by the integrity of certain nerves and (2) syndromes in which there are bilateral lesions. In the first group the extension of the growth is irregular, or certain nerves offer better resistance to the encroachment of the tumor. In some cases in the second group involvement of the motor nerves of the eye (the sixth especially) is exhibited, owing to destruction of the sella turcica, and in other cases there is early development of cancerous meningitis or metastasis, involving distant nerve structures, the so-called neutrophilic cancer.

DENNIS, San Diego, Calif.

Vegetative and Endocrine Systems

HIRSUTISM, HYPERTENSION AND OBESITY ASSOCIATED WITH CARCINOMA OF THE ADRENAL CORTEX, INTERMEDIATE PITUITARY ADENOMA AND SELECTIVE CHANGES IN THE BETA CELLS (BASOPHILS) OF THE HYPOPHYSIS. IRVING GRAEF, JOSEPH BUNIM and ANTONIO ROTTINO, Arch. Int. Med. **57**:1085 (June) 1936.

A case of the simultaneous existence of a pituitary and an adrenal tumor is reported. The patient, a girl aged 19 years, complained of increasing weakness and adiposity. Menstruation, which had begun at 12, was regular. The systolic blood pressure rose suddenly in a five day period from 124 to 148 mm. and fluctuated thereafter between 148 to 180 mm. The patient looked older than her years, and her protuberant abdomen seemed disproportionate to the wasted extremities. There was hypertrichosis of the face and extremities. As asthenia became rapidly progressive weight began to decrease. The urine contained 5,000

mouse units of estrogenic substances per liter, a greater quantity than that found in pregnancy. The patient died in coma. Autopsy revealed a large carcinoma of one adrenal. No trace of normal adrenal tissue could be seen in the affected gland. Although the pituitary gland was not enlarged, the anterior lobe contained a poorly defined miliary neoplasm, less than 1 sq. mm. in cross-section, consisting of nongranular, poorly defined cells arranged in irregular, discrete clumps. The authors cannot classify this other than as an indeterminate adenoma. The basophils were distorted and apparently agranular. The authors believe that the hypophysial growth was, in some as yet undefined way, secondarily related to the malignant growth in the adrenal. DAVIDSON, Newark, N. J.

RÔLE OF THE AUTONOMIC NERVOUS SYSTEM IN THE PRODUCTION OF PAIN. LOYAL DAVIS and L. J. POLLOCK, J. A. M. A. **106**:350 (Feb. 1) 1936.

Davis and Pollock studied the rôle of the autonomic nervous system in the production of pain in relation to afferent fibers either traveling with it or constituting a part of it. They propose to show that, so far as is proved, only the efferent fibers of the autonomic system itself are concerned with the production of pain and that such afferent fibers as travel with it belong to the spinal sensory system. In relation to pain from the extremities, they have previously shown that complete deafferentation of an extremity in man destroyed all forms of sensibility and that complete denervation of the peripheral nerves of an extremity in a decerebrate cat completely abolished all reflexes ordinarily observed as resulting from painful stimuli. The conclusion that there is no evidence for the existence of a sensory pathway through the autonomic system received recent confirmation in the work of Moore and Singleton. A type of referred visceral pain can be stopped by anesthetizing the area of skin into which the pain is referred. When, in some former experiments, Davis and Pollock were unable to stop pain produced by distention of the gallbladder by severing the intercostal nerves, they expressed the belief that this pointed to the existence of both true visceral, or splanchnic, pain and referred pain, confirming the work of Davis and of Ivy and Schrager. So far as the gallbladder is concerned, all forms of pain, referred or splanchic, are stopped by severing the right splanchnic nerve. Although it may be demonstrated that afferent painful impulses from the viscera are carried with the autonomic nervous system, the authors have no proof that the impulses are actually carried over autonomic neurons. In considering painful impulses from the head and diaphragm, a different situation is met. Painful impulses from the diaphragm travel over the phrenic nerve into the spinal cord by the cervical posterior roots and descend, probably by short pathways, to the level of the second thoracic segment. At that level a synapse with the cells in the anterolateral column occurs, and the impulses pass out through the cervical eighth and thoracic first, second, third and fourth anterior roots to the cervical portion of the sympathetic chain. Over efferent fibers the impulses are carried to the skin and other structures. A physiologic process then occurs, the nature of which is unknown. From the periphery the impulses then travel over the spinal sensory nerves into the spinal cord by the posterior roots. When the area of skin into which the pain is referred is rendered analgesic, although all other structures are intact, no pain is produced by experimental stimulation of the phrenic nerve or by disease of the diaphragm. If one considers the diaphragm as a visceral organ, it is obvious that the pain is not the result of peritoneal stimulation, since it occurs after section of the cord or of the thoracic posterior roots. Viscerosensory and visceromotor reflexes should be considered as nothing more than peritoneosensory and peritoneomotor reflexes, although there is no reason to believe that both types of reflexes should not exist. As in the case of pain in the face, it is seen that in pain referred from stimulation of the diaphragm the only proved contribution of the autonomic system to the production of pain is in its efferent arc. The only proved contribution of the autonomic nervous system to

pain is in relation to referred pain, in the production of which the efferent, not the afferent, fibers are utilized. In relation to pain both in the face and in the tip of the shoulder referred from the diaphragm there is physiologic proof to support this theory. In relation to pain in the face one is dealing only with autonomic efferent fibers in the cervical portion of the sympathetic chain. In pain in the tip of the shoulder referred from the diaphragm, severance of the appropriate purely motor anterior roots, which contribute to the cervical portion of the sympathetic chain, prevented diaphragmatic pain. The impulses of referred pain travel from the viscera with either autonomic or spinal sensory fibers to the spinal cord by way of the posterior roots. After passing over a synapse with cells in the anterolateral column, the impulses travel over preganglionic efferent fibers to the autonomic ganglia. Postganglionic fibers then carry the impulses to the skin, where the sensory end-organs are stimulated. Thus, an ordinary somatic painful impulse is produced, which travels over a spinal sensory nerve, enters the spinal cord by way of the posterior root and ascends in the lateral spinothalamic tract to a cortical level.

EDITOR'S ABSTRACT.

CLINICAL TESTS OF FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM. GEORGE E. BROWN, J. A. M. A. **106**:353 (Feb. 1) 1936.

According to Brown, clinical tests to measure responses of the autonomic nervous system have two broad purposes. The first is to determine the sensitivity or reactability of this nervous system in different functional disorders. In the conception of vagotonia and sympathicotonia, granted that an equilibrium or balance is maintained between the sympathetic and the parasympathetic mechanism, functional disorders do not follow this hypothetic anatomic balance. Cannon's conception of homeostasis seems to approach more closely the truth, in that the organism as a whole must be kept in a state of equilibrium from the broad physiologic aspect rather than from the narrow anatomic point of view. The determination of the fitness of the person to adapt himself to sudden changes in his environment, as carried out by tests similar to those used for aviators in the war, may make "fitness" a quantitative expression. Many functional disorders, then, represent a departure from this normally balanced physiologic state. This variation may be a diminished response, or hyporeaction, or an excessive response, or hyperreaction. The condition known as essential hypertension is one which, by virtue of an abnormal reactability of the vasomotor mechanism, illustrates an excessive response of the systemic blood pressure to stimulation. A similar illustration is found in Raynaud's disease and other forms of primary vasospastic neurosis. The response of the surface vessels of normal subjects to cold is constriction of the arterioles and capillaries, which produces faint grades of pallor, rubor or cyanosis of the skin. In both Raynaud's disease and essential hypertension there is a constitutional vasomotor status with excessive responses to certain forms of stress. The problem of clinical testing consists in subjecting the patient to a standardized form of stimulation in which the response can be compared with that of normal subjects. In vasospastic disorders the sharp responses in surface temperature to lowered temperatures, the slower recovery with warm temperatures and the sharp changes in color distinguish the abnormal from the normal reaction. In these functional hyperreactive states homeostasis is maintained, but at the expense of excessive reaction in the blood vessels. The extension of this concept in clinical medicine, then, evolves itself around the question of precise forms of tests and their interpretation. The second general purpose of this form of investigation is more specific than the first. The test is used to predict the dilating effects of interruption of the sympathetic nerves by operative measures. One prognostic test based on the response of vasoconstriction to fever determines the available vasodilatation. Another form of investigation does not involve stress per se but reproduces temporarily what is accomplished with operations that involve the sympathetic nerve tracts. Anesthetization of the sympathetic ganglia and peripheral nerves illustrates this point. These procedures determine quanti-

tative effects on the regional circulation by stimulating the vasomotor mechanism or by temporarily paralyzing the sympathetic pathways. When a disease or disorder can be measured in terms of disturbed function progress is inevitable. This conception is urgently needed in the large field of functional states. The broad conception of Cannon has done much to simplify matters, and as the normal state is visualized, the abnormal state becomes increasingly clear. The newer point of view of Dale is stimulating. He recommended the classification of the autonomic nervous system into nerves that are stimulated by epinephrine, which he designated as adrenergic nerves, and nerves that are stimulated by choline, which he designated as cholinergic nerves. This pharmacologic classification seems to offer more to the clinician than one based on an anatomic division. Facts are fragmentary, but the problem is assuming a logical and useful pattern. Brown predicts that the next major development in clinical medicine will be in the direction of the autonomic nervous system and its disorders.

EDITOR'S ABSTRACT.

INDICATIONS FOR OPERATIONS ON THE SYMPATHETIC NERVOUS SYSTEM. ALFRED W. ADSON, J. A. M. A. **106**:360 (Feb. 1) 1936.

Adson declares that indications for surgical treatment of diseases resulting from dysfunction of the sympathetic nervous system are based on the symptoms produced and the results obtained from interruption of the sympathetic pathways. The symptoms result from abnormal vasomotor stimuli and motor imbalance in the smooth musculature of the colon, sigmoid flexure, rectum, bladder, ureters and uterus. Since afferent sensations of pain travel through fibers that may be of sympathetic origin and these fibers run parallel with the postganglionic fibers to blood vessels and visceral organs, pain also is considered a symptom resulting from dysfunction of the sympathetic nervous system. The relief of symptoms obtained by one of the surgical procedures in the treatment of diseases produced by excessive vasomotor constriction results from the increased flow of blood to the extremity or organ involved. The motor imbalance resulting in excessive retention of urine in the bladder or ureters or the accumulation of feces, as observed in congenital megacolon, is corrected by decreasing the stimuli through interruption of a sufficient number of sympathetic fibers to balance the mechanism of retention with evacuation. Pain is relieved by the interruption of fibers carrying afferent sensations of pain, by increasing the flow of blood to the extremity or organ and by relieving spasm of smooth muscle. Though some of the sensations of pain travel along fibers in the sympathetic trunks, most of the relief obtained comes from the restitution of diseased tissue. Afferent impulses from this tissue are carried directly over spinal nerves. Dysmenorrhea undoubtedly results from excessive vasomotor stimuli and muscular spasm. The relief obtained by resection of the presacral nerves is the result of interruption of nerve fibers carrying sensations of pain, vasomotor stimuli and motor stimuli to the uterine muscles. Adson discusses the indications and selection of patients for and the expected results of operation on the sympathetic nervous system for the relief of peripheral vascular disease, Raynaud's disease, scleroderma, chronic arthritis of the rheumatoid type, essential hyperhidrosis, thrombo-angiitis obliterans, spastic and trophic lesions, essential hypertension, dysmenorrhea, motor imbalance and cord bladder. The postoperative care and period of convalescence following the extensive forms of sympathectomy are similar to those following laparotomy. The mortality on the whole compares with that of simple appendectomy. The mortality is higher for thrombo-angiitis obliterans than for other peripheral vascular diseases and averages 2 per cent. Dryness of the skin always follows operation for the relief of vasomotor spasm of the extremities. Presacral neurectomy, extensive rhizotomy and section of the splanchnic nerves, with removal of the two upper lumbar ganglia, result in paralysis of the urogenital trigon and interfere with the ejaculatory powers of the male, but they do not disturb potency or the libido.

These procedures interfere with virility, but they do not necessarily cause sterility. The occasional imperfect result obtained in the treatment of vasospastic diseases is due to incomplete operation, and this occurs most frequently with cervicothoracic sympathectomy, since it is easy to overlook accessory fibers. Sympathetic ganglia should be removed in conjunction with section of the postganglionic rami whenever it is possible, for the ganglion body which is preserved with the postganglionic ramus, even though the central connections have been severed, may have the property of exerting limited vasomotor influences. Horner's syndrome follows various forms of cervicothoracic sympathectomy, but the operation does not produce disfiguring symptoms when it is performed bilaterally.

EDITOR'S ABSTRACT.

BIOLOGIC EFFECTS OF PINEAL EXTRACT (HANSON): AMPLIFICATION OF EFFECTS IN THE YOUNG RESULTING FROM TREATMENT OF SUCCESSIVE GENERATIONS OF PARENT RATS. L. G. ROWNTREE, J. H. CLARK, ARTHUR STEINBERG and A. M. HANSON, J. A. M. A. **106**:370 (Feb. 1) 1936.

Rowntree, Clark, Steinberg and Hanson review the clinical investigations made on the effects of pineal extract (Hanson), from which it is apparent that unanimity of opinion is lacking in relation to the rôle of the pineal gland in biologic processes and to the part it plays in the clinical picture in tumor of this gland. One group of investigators expressed the belief that the pineal gland produces a secretion which inhibits the growth of the body and restrains mental and sexual development, while others, especially McCord, contended that the pineal gland stimulates growth and also sexual and physical precocity. On the clinical side, one group ascribed the endocrine features in cases of pineal tumor to underfunction of the gland and the other to overactivity. The success attending the authors' studies with the continuous administration of thymus extract (Hanson) to successive generations of parent rats, resulting in the remarkable precocity in the offspring in the third and succeeding generations, led them to attempt the same procedure with an extract of the pineal gland. To date, five successive generations of the strain of rats receiving the extract of the pineal gland have been under observation. In the first generation no effect was apparent other than moderate loss of weight and phenomena which suggest sexual excitation, such as increase in the size of the penis and early breeding. In the second generation there was definite retardation in growth, with mild precocity in gonadal development. In the subsequent generations, from the third to the fifth, there was accruing retardation in growth, with accruing acceleration in gonadal and bodily development. Precocious dwarfism is the outstanding result. The authors state further that it is evident that their results in the study of many hundreds of rats do not conform entirely to most of those reported in the literature. In common with the majority of workers they observed little or nothing of significance in the first generation receiving treatment. In the subsequent generations they consistently found dwarfism rather than stimulation of growth. Precocity, however, was observed in all animals from the third generation on, and this concerned both gonadal and bodily development. The resulting animal is small, often only half the normal size during the early weeks of life, and of precocious development, with genitalia suggesting those seen in association with macrogenitosomia praecox. In addition, the animals are physically weak and appear more irritable and nervous than normal. Blindness is a rather frequent occurrence in the rats treated with pineal extract. The cause is unknown.

EDITOR'S ABSTRACT.

THE PSYCHO-PHARMACOLOGY OF SODIUM AMYTAL IN CATATONIA. MELVIN W. THORNER, J. Nerv. & Ment. Dis. **82**:299 (Sept.) 1935.

A fall in systolic blood pressure, decrease in temperature, diminution in the basal metabolic rate, decrease in the oxidation of and absorption of dextrose by the

brain, exaggeration of the knee jerk and even ankle clonus are effects observed by narcotizing doses of sodium amytal. Thorner previously reported nine cases in which a transient Babinski response to plantar stimulation was noted during the intravenous administration of the drug at the moment unconsciousness was about to appear. The drug seems to act as an inhibitor of the activity of the nerve cells, affecting the various divisions of the nervous system in the reverse order of their phylogenetic appearance. In catatonia and superinhibited states the drug appears to act in inhibiting the superinhibition. HART, Greenwich, Conn.

A CASE OF POSTOPERATIVE TETANY WITH SERIOUS MENTAL DISTURBANCES. H. BAONVILLE, J. LEY and J. TITECA, Ann. méd.-psychol. **92**:26 (June, pt. 2) 1934.

The tetanic syndrome due to parathyroid insufficiency is well known, but tetany accompanied by mental symptoms is rare. Frankl-Hochwart (1890), Schultze (1897), Luther (1901), Lapinsky (1907) and Lemaire (1925) made observations on psychic disturbances in patients with tetany but failed to describe them in detail. Recently, there have been several reports of cases in which transitory mental symptoms occurred. The present case is that of a woman aged 40, with a family history of no significance, who showed hyperthyroidism after the birth of her first child. In spite of treatment the symptoms increased in severity, and subtotal thyroidectomy was performed, with the patient under spinal anesthesia. Fifteen days after the operation the first symptoms of tetany were noticed, consisting of pathognomonic cramps and rigidity and pain in the limbs and the muscles of respiration. A few days after this there developed polymorphic delirium and hallucinations. About one month after operation the patient attempted suicide by hanging but failed to accomplish her purpose. Physical examination yielded no especially remarkable results except roughening of the long bones, as seen by roentgen ray. The serum calcium content of the blood was 6 mg., the erythrocyte count 6,520,000, the leukocyte count 8,900 and the hemoglobin content 90 per cent. The cerebrospinal fluid and urine were essentially normal except for an increase of bile pigment in the urine. Neurologic examination showed diminution of cutaneous sensation, feeble cutaneous reflexes and equal and active pupils on the two sides, with no trace of exophthalmos. There was no indication of cerebellar or meningeal involvement.

Mental examination showed poor orientation as to time. Memory for remote events was better than that for recent events. Voluntary attention was poorly sustained, but the intellectual faculties did not seem to be affected except that all cerebral activity was greatly slowed. It was necessary to repeat questions several times before obtaining an answer. During tetanic crises recrudescence of all the mental troubles was observed. Hallucinations of sight and sound were marked. The patient appeared terrified and displayed paranoid phenomena.

The appearance of tetany was irregular and did not differ from that observed after extirpation of the parathyroid glands. The treatment consisted of intravenous injection of calcium gluconate and administration of cod liver oil and parathyroid extract in a dose equivalent to 6 mg. a day. After a week of this treatment the tetanic seizures became less frequent, and during the intervals the patient appeared to be normal physically. However, she displayed mental symptoms, such as defect in memory and great anxiety for her family. After one and a half months of hospitalization the tetany disappeared almost entirely. One month later, during an attack of otitis media, there was recurrence of tetany and of the mental symptoms. These disappeared simultaneously. Three months after the onset of the mental symptoms the patient returned to her family, showing no signs of tetany or mental trouble, although the parathyroid therapy had been gradually withdrawn. Seven months after operation the patient was still free from parathyroid and thyroid disturbance. The general health was excellent.

MOORE, Boston.

Cerebrospinal Fluid

COMPARATIVE DEXTROSE CONTENT OF LUMBAR AND CISTERNAL CEREBROSPINAL FLUID. ABRAHAM LEVINSON and DAVID J. COHN, Am. J. Dis. Child. **51**:17 (Jan.) 1936.

Levinson and Cohn studied two groups of patients: those with diseases other than meningitis and those with some form of meningitis. Experiments were made with dogs. Twenty-three specimens of cisternal and lumbar spinal fluid from nineteen patients who did not have meningitis and forty-nine specimens of fluid from thirty-eight patients with meningitis were studied. In the group of patients who did not have meningitis the dextrose content of the cisternal fluid was either equal to or slightly higher than that of the lumbar fluid. In patients in whom there was no pathologic change in the central nervous system the dextrose content averaged 57 mg. per hundred cubic centimeters and that of the cisternal fluid 60 mg. On the other hand, in patients with tuberculous meningitis and patients with meningococcic meningitis who were not treated, the dextrose content of the lumbar fluid was always reduced. The dextrose content of the cisternal fluid, while usually lower than normal, was not as low as that of the lumbar fluid. In some cases the dextrose content of the cisternal fluid was within normal range, in spite of marked diminution of dextrose in the lumbar fluid. Values for the dextrose content of cisternal and lumbar fluids in patients with meningococcic meningitis who had received treatment were more nearly normal than those in patients who had not been treated, while the difference between the content in the two fluids was less marked. In a small number of cases of nonmeningococcic purulent meningitis there was a small amount of dextrose in both the cisternal and the lumbar fluid. The authors believe that determination of the dextrose content in the lumbar fluid is more reliable in the diagnosis of meningitis than that in the cisternal fluid. It is believed that in cases in which the prognosis is poor the cisternal fluid, as well as the lumbar fluid, shows less dextrose, but the authors think that combined puncture for prognostic reasons is not advisable, in view of the complications resulting from cisternal puncture.

WAGGONER, Ann Arbor, Mich.

THE FILTERABLE CALCIUM OF BLOOD SERUM: I. A COMPARISON OF FILTERABLE CALCIUM OF SERUM AND TOTAL CALCIUM OF CEREBROSPINAL FLUID IN NORMAL, HYPERPARATHYROID AND HYPOPARATHYROID STATES. RAYMOND GREGORY and MARIE ANDERSCH, Am. J. M. Sc. **191**:263 (Feb.) 1936.

Daily simultaneous determinations of the total and filtrable calcium of the serum and of the calcium content of the spinal fluid were made in two cases of hyperparathyroidism and in two of hypoparathyroidism to ascertain whether there was any variation in the calcium of the spinal fluid and the filtrable calcium of the serum during a period of weeks. In one case of hyperparathyroidism, in which the total calcium content averaged 15.3 mg. per cubic centimeter, the filtrable calcium content of the serum averaged 7.2 mg. Six estimations of the calcium content of the spinal fluid varied from 5.5 to 6.4 mg., averaging 5.8 mg., which is considerably lower than the average value (7.2 mg.) for the filtrable calcium content of the serum in this case. In a second case of hyperparathyroidism the calcium content of the spinal fluid varied from 4.4 to 5 mg., whereas the amount of filtrable calcium in the serum averaged 7.3 mg. In both cases of hypoparathyroidism the results indicated that it is principally the filtrable calcium of the serum which decreases in parathyroid tetany. The amount of filtrable calcium in the serum and that of the total calcium in the spinal fluid are usually practically equal over the normal range of values for serum calcium. Wide variations in the filtrable calcium content of the serum may occur without any change in the calcium content of the spinal fluid. The spinal fluid probably does not represent an ultrafiltrate of the plasma so far as calcium is concerned.

MICHAELS, Boston.

A Routine Diagnostic Procedure for the Patient Who Enters the Hospital in Coma. Philip Solomon and Charles D. Aring, Am. J. M. Sc. **191**:357 (March) 1936.

Of 1,167 patients who entered the hospital in coma in 1933, the condition was diagnosed correctly at the time of admission in 1,101 (94 per cent). Of 477 nonalcoholic patients, the diagnosis was incorrect on admission in 64 (13 per cent). The lack of an adequate history was largely responsible in 45 per cent of the cases in which an incorrect diagnosis was made. The history was of diagnostic importance in 80 per cent of cases of coma of nonalcoholic origin. The importance of the physical examination is stressed, as mistakes in diagnosis are made because of an inadequate examination of patients who are considered to be alcoholic. Of the 5 patients who were thought to be in coma due to alcoholism, 4 had a cerebral condition and 1 lobar pneumonia. Patients who enter the hospital in coma should be treated as having an emergency condition. Roentgen examination would have been of service in making the correct diagnosis in 15 cases, or in 23 per cent of all the cases in which an incorrect diagnosis was made. Roentgenograms of the skull should be taken as a routine for comatose patients who show evidence of injury. Laboratory examination other than lumbar puncture was of diagnostic value in 107 cases (9 per cent) of the total series. In 174 cases, or 15 per cent of the total number, lumbar puncture was of critical diagnostic significance. If lumbar puncture had been performed, correct diagnosis would have been made in 16 (24 per cent) of cases in which it was incorrect. Lumbar puncture should be performed as a routine in all cases of injury (except during shock), cerebral vascular accident and convulsions, in the presence of signs of increased intracranial pressure or meningeal irritation and in all cases in which the diagnosis is obscure.

Michaels, Boston.

Factors Influencing the Absorption of Spinal Fluid. Lewis Weed, Am. J. Physiol. **114**:40 (Dec.) 1935.

By adding colloids, such as a solution of casein or gelatin, to the subarachnoid fluid, Weed found the rate of absorption to be retarded. Little effect on the rapidity of absorption was produced by adding Locke's or other crystalloid solution to the fluid. This seems to confirm the hypothesis that one of the determinants of the rate of absorption is the difference in tension between the colloids of the blood and those of the spinal fluid. Normally, the crystalloid content of the blood and that of the spinal fluid are about the same, so that no pressure differential exists. However, the normal spinal fluid is devoid of colloid; so the colloidal osmotic pressure of the spinal fluid is zero. By adding a solution of gelatin or casein to the spinal fluid, a positive colloid osmotic tension is produced, thus effectively reducing the difference between the blood and the cerebrospinal fluid tension and to that extent retarding the rate of absorption. Another factor in effective subarachnoid fluid pressure is the hydrostatic difference between the subarachnoid fluid pressure and the intracranial venous tension. The total effective pressure is obtained by adding these two differences (i. e., the difference in tension between the colloids of the blood and those of the spinal fluid plus the difference between the intracranial venous pressure and the subarachnoid pressure); the ratio of this total effective pressure to the amount of fluid absorbed in a given time is a constant, whatever additions are made to the subarachnoid fluid. This means that the greater the effective pressure the greater the absorption, and it tends to confirm the hypothesis of the hydrostatic nature of the pressure forces concerned in absorption of spinal fluid.

Davidson, Newark, N. J.

Cerebrospinal Hydrodynamics: V. Studies of the Volume Elasticity of the Human Ventriculo-Subarachnoid System. Jules H. Masserman, J. Comp. Neurol. **61**:543 (June) 1935.

A special apparatus was constructed which made possible (1) the removal of spinal fluid from the lumbar portion of the subarachnoid space at any desired

rate and in any amount within physiologic limits, (2) the reinjection of this fluid or of modified Ringer solution into the lumbar space with the same precise control of rate and volume, (3) accurate manometric determinations of the resultant changes in subarachnoid pressure and (4) study of cerebrospinal hydrodynamic reactions on tilting the subject from a sitting through a lying to a partial head-down position. The results of various experiments performed with this apparatus on a group of forty persons are reported in this article. Masserman concludes that the coefficient of meningeal volume elasticity remains fairly constant in the same person for the drainage of a given amount of cerebrospinal fluid, with the subject in any one position. There is a corresponding constancy of this coefficient throughout fractional drainages. Marked deviations in the index of change of cerebrospinal fluid pressure may be of clinical significance, but the index varies widely among persons with no organic disease of the nervous system.

FRASER, Philadelphia.

CRYSTAL-FORMATIONS IN THE SPINAL FLUID AND THEIR DIAGNOSTIC SIGNIFICANCE. K. ZEINER-HENDRIKSEN, J. Neurol. & Psychopath. **16**:111 (Oct.) 1935.

Favorable conditions for the formation of crystals exist in the spinal fluid because of the greater content of electrolytes than of organic ingredients. Under pathologic conditions the factors necessary for crystallization are altered, Zeiner-Hendriksen therefore supposed that the type of crystals formed might be of diagnostic value. Two types of crystals are found in the normal spinal fluid: (1) pyramidal crystals of sodium chloride and (2) needle-like formations. Examination of the crystals in the fluid in cases of dementia paralytica reveals that crystals of type 1 are transformed into shapes of stars or daggers and that crystals of type 2 assumed the form of oak trees, fir trees, bushes or rosettes. With treatment with malaria the crystal picture gradually changed in a normal direction. On the basis of these observations in sixty-six cases of dementia paralytica Zeiner-Hendriksen believes that the crystal formations in this disease may be of diagnostic value. In other cases of organic and functional nervous disease the spinal fluid was similarly examined, but the results are not stated. N. MALAMUD, Ann Arbor, Mich.

STUDIES ON PERMEABILITY IN LIQUORRHEA. F. ROEDER, Arch. f. Psychiat. **103**:159 (March) 1935.

Liquorrhea nasalis usually occurs in cases of tumor of the brain, especially of the pituitary, and occasionally in hydrocephalus. The pathway by which the cerebrospinal fluid escapes has been thought to be through the sheaths of the olfactory nerve by perforation of the lamina cribrosa and sometimes by erosion of the sella turcica.

Roeder reports a case of congenital hydrocephalus in an adult, who began to show this phenomenon fourteen days before his admission to the hospital. The cerebrospinal fluid escaped from the nose at the rate of from about 50 to 60 cc. a day. It was clear and contained 1 cell per cubic millimeter; the total protein was 21.6 mg. per cubic centimeter, globulin 7.2 mg. and sugar 76 mg. Studies on permeability were undertaken by the Walter bromide method. The determinations were made beginning on the first day after the administration of bromides and continuing for sixteen days (bromides were given daily for five days). The quotient continued to be fairly consistent, with an average of 1.19 (normal, about 3). An increase in permeability was also noticed in the cholesterol content, that of the blood being 76.9 mg. per hundred cubic centimeters and that of the cerebrospinal fluid from 0.5 to 0.6 mg. or practically twice that of the normal. This, however, was not found to be the case for the permeability to colloid substances, such as typhoid vaccine and similar materials. The conclusion is that, whereas certain conditions may cause an increased permeability to crystalloids, they may not produce the same effect in relation to colloids. W. MALAMUD, Iowa City.

Treatment, Neurosurgery

USE OF TYPHOID VACCINE IN TREATMENT OF CHOREA: ITS POSSIBLE DANGERS. RACHEL ASH and NATHAN EINHORN, Am. J. Dis. Child. **50**:879 (Oct.) 1935.

Ash and Einhorn assume that chorea is a manifestation of rheumatic infection and call attention to the frequency of carditis in these cases. In some of their cases they believe that typhoid vaccine therapy definitely aggravated the patient's condition when the patient had active carditis. They state that during the febrile reaction following intravenous injection of typhoid vaccine there is depression of granulocytes and that this method of therapy should be checked by frequent determinations of the white blood cell count. They also conclude that typhoid vaccine therapy does not prevent recurrence of chorea. In the authors' experience the sedimentation test has proved the best single laboratory guide in the presence of rheumatic infection, but its meaning must be evaluated. In the presence of an increased sedimentation rate, conservative measures in the treatment for chorea are indicated.

WAGGONER, Ann Arbor, Mich.

THE EFFECT OF THERAPY ON NERVE DEGENERATION IN PERNICIOUS ANEMIA. EDWARD S. MILLS, Am. J. M. Sc. **191**:72 (Jan.) 1936.

Therapy for pernicious anemia to be considered adequate must meet the following requirements: (1) The erythrocyte count must be normal at all times; (2) the modal erythrocyte count must be at or below the normal value, and macrocytosis is an indication of failure, and (3) therapy must be increased at once if there is any untoward change in the patient's status. Five cubic centimeters a week of a potent liver extract given intramuscularly, will suffice in many cases. Of the forty-five patients given treatment during seven years only one failed to show evidence of subacute combined degeneration of the cord at the time of the first visit. Forty-four patients showed diminution in two point discrimination or in vibration sense, and less than half, alterations in the tendon reflexes or other signs of involvement of the cord. In 47 per cent of the twenty-eight cases in which adequate treatment was given, improvement in the subacute combined degeneration was shown, and in an additional 40 per cent there was no tendency to progress. In only 17 per cent of the seventeen cases in which inadequate treatment was given improvement was shown, while in 82 per cent there was progressive degeneration. The improvement can be explained only on the basis of degeneration of nerve tissue without actual destruction. It is concluded that degeneration of the spinal cord is present in cases of pernicious anemia, and if treated adequately it rarely tends to progress.

MICHAELS, Boston.

DEMENTIA PARALYTICA: RESULTS OF TREATMENT WITH DIATHERMY FEVER. S. H. EPSTEIN, H. C. SOLOMON and I. KOPP, J. A. M. A. **106**:1527 (May 2) 1936.

Epstein, Solomon and Kopp state that a review of the literature dealing with the results of treatment for dementia paralytica with fever produced by diathermy and related mechanical modes of hyperpyrexia indicates that of a total of six hundred and forty-eight cases reported between 1929 and 1935 good remissions were reported in 27 per cent. In their series of thirty-three patients who were treated with diathermy between February 1931 and February 1934, according to their analysis made in February 1935, eight patients were improved and working, and an additional seven patients were improved but were not self-supporting. Four patients, while remaining hospitalized, were known to be improved. Four patients were living but were not improved, and ten patients had died. In one case there was a definite clinical relapse with reversion to a positive serologic reaction four years after diathermy fever therapy. Of the fifteen patients who were clinically improved, eight, or approximately one-half, had normal or nearly normal spinal fluids. It seems possible to the authors that their results in the total group

of cases would have been much better if the diathermy treatment had been more prolonged and at a higher temperature level. The longevity figures based on the percentage of patients who died within two years after treatment indicate that 27 per cent of the series of patients treated with diathermy died within two years. This is compared with the values previously reported of 14.8 per cent for the series in which malaria treatment was given and 13.5 per cent for the series in which tryparsamide was administered. A comparative study of the clinical results among patients treated with malaria, artificial hyperpyrexia, including diathermy, and tryparsamide indicates that the best remissions were obtained in a little more than 45 per cent of the patients treated with malaria and 42 per cent of the patients treated with tryparsamide, as compared with 27 per cent of the patients treated with artificial hyperpyrexia. A comparative study of the serologic results indicates that about 22 per cent of the patients in the series treated with diathermy showed a normal reaction of the spinal fluid after treatment, as compared with 37 per cent in the series of patients treated with malaria and tryparsamide.

EDITOR'S ABSTRACT.

INSULIN TREATMENT OF DRUG ADDICTION. M. P. CHEN, Y. L. CH'ENG and R. S. LYMAN, J. Nerv. & Ment. Dis. **83**:281 (March) 1936.

Chen, Ch'eng and Lyman used insulin in the treatment of five persons addicted to the use of drugs. The patients were first studied while receiving the satisfying dose of morphine and then after sudden and complete withdrawal of all opiates. When symptoms of craving began to appear, insulin in doses of from 20 or 30 units every three hours, with phenobarbital and food, was given. The symptoms of abstinence disappeared after from three to five days of treatment with large doses of insulin. During the period the patient was allowed to eat as much as he wanted. Estimation of the blood sugar during the period showed never less than 78 mg. per hundred cubic centimeters. The insulin produced general physical relaxation, accompanied by lowering of the blood sugar, changes in the blood fats, a slight shift toward alkalosis, reduction in the calcium and potassium contents of the blood and gain in weight. The patients remarked that, whereas in previous periods of abstinence they craved the drug, under the insulin regimen they craved only food. Food is symbolic of health and the starting-point for mental and social anabolism. One patient who had almost no capacity for self-discipline and who feared the treatment failed to secure benefit from it. He was the only one to vomit when given insulin.

HART, Greenwich, Conn.

THERAPEUTIC QUARTAN MALARIA IN THE TREATMENT OF NEUROSYPHILIS AMONG NEGROES. GEORGE C. BRANCHE, J. Nerv. & Ment. Dis. **83**:177 (Feb.) 1936.

A high percentage of Negroes of the North American continent, particularly those possessing a preponderance of African strain, have a natural resistance to tertian malaria. Immunity to quartan malaria is less prevalent among this group. Branche inoculated thirty-six Negro patients with the quartan malarial organism, with success in 91 per cent. In a group of twenty-two Negro patients inoculated with the tertian malarial organism there were "takes" in only 14 per cent. In none of the patients treated did jaundice or convulsive seizures develop, nor did any case of severe anemia occur. The blood pressure seldom dropped below 100 systolic. Patients showing excessive temperature were brown, light brown or mulatto. Those showing only slight fever, often without chills, more nearly approached the African type. Branche believes that the temperature obtained in quartan fever is higher than that in the tertian form. In most cases quartan fever will terminate spontaneously if allowed to do so, but the use of quinine becomes necessary in about half the cases. When this drug was used, however, there was a peculiar tendency to relapse. Branche considers that the longer period of rest between the febrile attacks may be a distinct asset in giving the patient time to recuperate. Curiously, continued inoculation with the quartan plasmodium

in the few persons who failed to respond to this strain with elevation of temperature seemed to cause clinical and serologic improvement quite as significant as that noted in patients who experienced actual malarial paroxysms.

HART, Greenwich, Conn.

MANAGEMENT OF SKULL FRACTURES: HOW CAN THE HIGH MORTALITY RATE BE REDUCED? HARRY E. MOCK, New England J. Med. **214**:625 (March 26) 1936.

In 92 per cent of 200 cases of fracture of the skull entered in Dr. Mock's service at St. Luke's Hospital, Chicago, the diagnosis was proved. In the remaining instances the condition was so obviously fracture of the skull that the cases had to be included. The total death rate was 18.2 per cent. There was a death rate of 46 per cent in the first twenty-four hours, and one of 38 per cent in the first seven days. It has been proved that 45 per cent of deaths occur in the first twenty-four hours. A high mortality rate can be reduced by proper early management of the condition.

In fracture of the skull, shock should be treated first and suture of lacerations after one has had a better chance to cleanse and free the wound from débris and to make sure that a compound fracture does not exist. Only occasionally is there a severe hemorrhage which endangers life and requires the immediate attention of the surgeon, even in the presence of shock.

The least possible movement of the patient is the chief essential in the presence of injury to the head, especially when cerebral shock is present. Roentgenograms should be made in every case of injury to the head except when the patient is in shock. In a case of fracture of the skull, operation immediately or within a few hours is seldom indicated. In 28 of 30 cases of fracture of the skull immediate operation resulted in death. In all of 15 cases in which subtemporal decompression was performed in the first seven hours death followed. Every injury to the head should be treated as serious until proved otherwise.

Forty per cent of deaths occur on from the second to the seventh day. Respiratory and cardiac failure cause the great majority of deaths in this period. The next commonest cause of death is pneumonia. Meningitis causes less than 5 per cent of the deaths. Multiple injuries, diabetes, syphilis, alcoholism and old age are marked contributing factors to the death rate.

Dehydration, started early after shock and persisted in, will reduce the number of fatalities. In about 55 per cent of the cases its early and proper employment has prevented the condition from passing into one in which lumbar puncture or operation is required.

The earlier lumbar puncture is performed when indicated the lower the death rate. A lumbar puncture made early, before medullary compression has developed, is often extremely spectacular in its results. Increased intracranial pressure persisting after early dehydration requires lumbar puncture.

In 10 per cent of the cases in Mock's series operation was required. The longer the operation can safely be postponed the lower is the death rate following operation. Subtemporal decompression is seldom indicated. In 942 cases there were 27 such operations and 22 deaths.

The high mortality rate from fracture of the skull can be reduced by observing the commonplace principles discussed in the paper and by proper application of general and special therapeutic measures.

MOORE, Boston.

Muscular System

SYNDROME OF DIFFUSE MUSCULAR HYPERTROPHY IN INFANTS CAUSING ATHLETIC APPEARANCE: ITS CONNECTION WITH CONGENITAL MYXEDEMA. ROBERT DEBRÉ and G. SEMELAIGNE, Am. J. Dis. Child. **50**:1351 (Dec.) 1935.

Debré and Semelaigne report two cases of intellectual and physical retardation and muscular hypertrophy of the athletic type in infants, accompanied in one

instance by muscular hypertonia. They call attention to the similarity between their cases and those reported previously by de Lange (Congenital Hypertrophy of the Muscles, Extrapyramidal Motor Disorders and Mental Deficiency: Clinical Entity, *Am. J. Dis. Child.* **48**:243 [Aug.] 1934). They believe that the syndrome described is similar to that described by de Lange. In one of the children the condition was remarkably benefited by thyroid therapy, and they claim that congenital athyroidism may cause this clinical syndrome. They advise systematic treatment with thyroid in such cases, as this may not only benefit the patient but may help solve the question of the pathogenesis of the syndrome.

WAGGONER, Ann Arbor, Mich.

THOMSEN'S DISEASE (MYOTONIA CONGENITA). BERNARD I. COMROE, Am. J. M. Sc. **189**:714 (May) 1935.

In view of the paucity of reports in the American literature of families with Thomsen's disease, the case of a youth aged 19 is described, together with a concise résumé of the important features of the disorder. Stiffness of the musculature on voluntary movement or effort is the chief characteristic. A biopsy specimen from the left gastrocnemius muscle showed loss of compactness of each fiber, faint cross-striations, prominence of the longitudinal fibrils and an increase in the size of the longitudinal fibers. No beneficial results were obtained with the administration of 25 Gm. of amino-acetic acid daily for seven days. However, the use of ephedrine sulfate, ⅜ grain (0.024 Gm.) three times a day by mouth, resulted in marked subjective improvement.

MICHAELS, Boston.

INFLUENCE OF LARGE DOSES OF POTASSIUM CHLORIDE ON MYASTHENIA GRAVIS. L. P. E. LAURENT and W. W. WALTHER, Lancet **1**:1434 (June 22) 1935.

Laurent and Walther report that potassium chloride given in large doses by mouth causes a demonstrable improvement in myasthenia. In small repeated doses it is a useful adjuvant to the di-methylcarbamic ester of 3-oxyphenyl-tri-methylammonium methylsulfate. The action of physostigmine and its analog the di-methylcarbamic ester of 3-oxyphenyl-tri-methylammonium methylsulfate in the relief of myasthenic symptoms was described by Walker. It was suggested that the physostigmine acts by delaying the destruction of acetylcholine by choline esterase at the motor nerve ending. Feldberg and Vartiainen, in the course of experiments on the superior cervical ganglion of the cat, found that the addition of potassium chloride to the perfusing solution stimulated the ganglion cells. They also found that a dose of potassium chloride not large enough to stimulate the ganglion cells directly raised their excitability to preganglionic stimuli, to acetylcholine and to other chemical stimulants. Further, they found that physostigmine perfused through the ganglion in weak concentration strongly sensitized the ganglion cells to injections of acetylcholine, lowering the threshold dose from eight to twenty times.

In view of these findings Laurent and Walther investigated the influence of potassium chloride in cases of myasthenia, using doses sufficiently large to raise the potassium level of the blood significantly. They first determined the level of potassium in the blood plasma of ten normal subjects and of six subjects with myasthenia. No definite abnormality was found in patients with myasthenia. Estimation of the amount of potassium in the plasma an hour after the ingestion of potassium chloride showed a considerable increase in each case. The best results were obtained with large doses of potassium chloride, but the authors did not consider the results as good as those obtained with injection of the di-methylcarbamic ester of 2-oxyphenyl-tri-methylammonium methylsulfate. However, they found that a dose of potassium chloride taken before the action of the drug had ended relieved the feeling of exhaustion and to some extent prolonged the improvement which it brought about.

WATTS, Washington, D. C.

A Special Form of Feeblemindedness Associated with Myosclerosis: Contribution to the Study of Mental Disturbances Accompanying Myopathy. Carlo Berlucchi, Riv. di pat. nerv. **44**:453 (Nov.-Dec.) 1934.

Berlucchi describes a special form of feeblemindedness associated with myosclerosis which he considers to be related to the forms of muscular dystrophy. He asserts that muscular dystrophy is a disease involving not the muscular system alone but various other organs and systems. Many patients with muscular dystrophy are free from mental complications. In a small number of cases, such as those Berlucchi describes, the mental disturbances are much more serious and assume the character of extreme feeblemindedness. In such cases the muscular dystrophy has a rapid course, and severe involvement of the lower extremities with flexion attitudes often results, accompanied by marked muscular retraction. Pseudodystrophy in these cases is not striking.

A few cases of feeblemindedness of this type associated with myosclerosis are described in the literature, but the condition has never been studied from the pathologic standpoint, nor has it been clearly differentiated from other forms of feeblemindedness associated with motor disturbances.

Berlucchi concludes that the entity which he describes differs from forms of idiocy associated with cerebral lesions for the following reasons: (1) Several cases of feeblemindedness associated with myosclerosis have appeared in families in which other members were afflicted with common forms of muscular dystrophy and (2) in the cases in his series characteristic pathologic changes occur. The variety he reports should, in his opinion, occupy an autonomous position in the group of cases of arrested mental development.

The involvement of the mental processes is severe from earliest infancy. On the other hand, the symptoms of muscular dystrophy manifest themselves generally after the seventh year. Before the age of 7 years the patient is considered to have an advanced form of feeblemindedness. As an additional symptom Berlucchi reports the occurrence of high blood pressure and disturbances in the vegetative mechanisms, leading to pronounced vasomotor imbalance.

From the pathologic changes the author concludes that the motor disturbances are the result of primary involvement of the muscular system. The pyramidal tracts and cells of the anterior horns are not severely involved. On the basis of the data given, he considers himself justified in establishing a special form of feeblemindedness associated with myosclerosis which belongs to the common group of muscular dystrophy and is distinct from the usual forms of idiocy.

Ferraro, New York.

Cerebellum and Brain Stem

Cerebellar Abscess from the Otologic, Neurologic and Ophthalmologic Points of View. J. Ramadier, R. Caussé, André-Thomas, J. A. Barré and E. Velter, Rev. d'oto-neuro-opht. **13**:1 (Jan.); 85 (Feb.) 1935.

This article is a comprehensive report to the eighth congress of the *Sociétés françaises d'oto-neuro-ophthalmologie,* held in Nice, France, in April 1935. "The contributors united their efforts, submitted proofs to each other, discussed and criticized. It is without doubt the first report on abscess of the cerebellum that has been conceived in this spirit of collaboration and scientific fusion."

The report is divided into three parts: (1) symptoms and diagnosis, (2) pathways of propagation of infection and lesions produced and (3) treatment. Combined statistics based on the reports of autopsies indicate that the proportion of cases in which abscess of the brain was observed in the total number of autopsies is, on the average, 0.24 per cent. Abscess of the cerebellum is still more rare, 30 per cent of abscesses of the brain being located in the cerebellum. The disease is most frequent in the third decade of life. While abscess of the cerebellum may be due to traumatism or other causes, in practically all cases it is of auricular

origin. It is extremely rare for a cerebellar abscess to follow uncomplicated acute otitis, the usual complication being extradural abscess or thrombophlebitis. In cases of abscess complicating chronic otitis the usual intermediate complication is labyrinthitis. Cases of abscess located in the side of the cerebellum opposite that of the diseased ear are so rare that they may be disregarded. While a single abscess is most frequent, multiple abscesses are not exceptional and may be present in both the cerebrum and the cerebellum.

The symptomatology of abscess of the cerebellum is extremely rich and varied. The patient has a history of auricular infection that may have involved the labyrinth or the cellular structure of the bone and have extended to the meninges. Whatever the pathway to the brain, a more or less extensive meningeal infection results; the pia is thickened; the interlobular septums are more and more thickened as one approaches the accumulation of pus, and microscopic inflammatory nodules are observed along the vessels, not only in the septums but in the cortex and white substance. The diseased lobe is edematous, and the vermis, bulb and, indeed, all the structures in the cerebellar fossa are displaced; hence, there is disturbance of the paracerebellar nuclei, especially the vestibular centers, and even of the cerebellar structures of the opposite side. The abscess may be deeply or superficially situated. If located in the central white substance it may irritate or destroy fibers from the cortex, the dentate nucleus or the roof nucleus. To this must be added the effects of intracranial hypertension. A patient with abscess of the cerebellum has not a purely cerebellar condition; he has always a cerebellolabyrinthine involvement. The labyrinthine factor is contributed by the lesion of the internal ear and by repercussions on the labyrinthine nuclei and the connections between the cerebellum and the labyrinth.

Some general symptoms of abscess of the brain, considered in connection with the past history of auricular disease, are of major importance in the diagnosis. These symptoms are hypothermia, bradycardia, somnolence, diminution of respiratory exchange, hypotension and hyposensibility to sensory stimuli. The pulse rate is influenced somewhat by the intracranial hypertension but perhaps more by the edema and its repercussion on the bulb and the centers of the vagus (pneumogastric) nerve. Headache is a constant symptom; it varies in intensity with the stage of the disease but is not absent even during the latent period of the abscess. The location of the headache is not reliable as a localizing symptom. Hypertension, edema and distention of the meninges play a part in its production. One of the most typical general signs of abscess of the brain is rapid and marked loss of weight, especially when it occurs in connection with chronic otitis. In association with abscess of the cerebellum, nausea and vomiting (of the cerebral type) are not particularly frequent and are more often present in an advanced stage. Changes of character, slowness of reactions, somnolence and yawning, gradually proceeding to a stuporous state, are less marked than in connection with cerebral abscess. The important features in the meningeal syndrome are the existence and nature of the meningeal reaction. The question can be resolved only by repeated cytologic, bacteriologic and chemical examinations of the cerebrospinal fluid. In a patient with no meningeal signs cloudiness of the cerebrospinal fluid points to meningitis secondary to abscess. Likewise, in a patient in a state of torpor one must assume that if the fluid is sterile and contains only from 5 to 600 cells the condition is caused not by the meningeal state but by a deeper-seated complication, probably an abscess. In general, hypertension of the cerebrospinal fluid is more frequently encountered and more marked in abscess of the cerebellum than in abscess of the cerebrum. The danger of spinal puncture for a patient with the former condition may be minimized by practicing this procedure with the subject in the recumbent position.

Among the less important diagnostic indications of abscess of the cerebellum is Brock's sign. It should be remembered, however, that in cases of brain abscess stiffness of the neck is rare. In the early stages of abscess signs of meningeal irritation are absent, but later stiffness of the neck and Kernig's sign

are present and are correlated with the results of examination of the fluid. Papillary stasis is more frequently met in abscess of the cerebellum than in abscess of the cerebrum. Lillie found that progressive increase of stasis indicated activity of the encephalitic process and that in cases in which operation was performed at this period the mortality was high. In abscess of the cerebellum, which is practically always secondary to otorrhea, simple enumeration of the leukocytes does not furnish valuable information, but study of Schilling's hemograms after intervention yields important data. Only repeated examinations are of value.

The intensity of the various cerebellar signs varies with the stage of evolution of the abscess; in the majority of cases they are discrete and predominate in one member, usually the upper limb on one side. It cannot be said in any given case that no cerebellar signs exist unless the examination is methodical and detailed. When the patient is confined to bed only the activity of the members can be explored, and when torpor is present clinical investigation is limited to examination of tonus. In observing station and gait the impression received is that of a person who fears to lose his equilibrium rather than that of an intoxicated man who has lost all control. These troubles, sketchy at first, become more marked as the disease progresses, owing to participation of the vestibular apparatus. Disturbances of tonus often appear earlier than other signs. In disease of the cerebellum the limb is more passive (diminution in the resistance of antagonists)—hence the term hyposthenia (André-Thomas). Extensibility may be simultaneously increased in association with abscess of the cerebellum, but in that case the cerebellum is not the sole cause. In the obscure pyramidal syndrome it is exceptional for passivity to exist without extensibility, in that lesion, however, there are other signs, and the passivity is crossed in relation to the cerebral lesion. All joints must be examined. Hyposthenia modifies the tendon reflexes by causing an increase in the amplitude of the movement of extension and oscillation before the limb becomes immobile again. It is probable that catalepsy does not result from disturbance of the cerebellum or at least from exclusive involvement of this organ. It is only at an advanced stage, when the abscess has attained considerable size or is located near the median line and the vermis, that the symptoms become bilateral; even then they predominate on the side of the disease. To explain the rarity of cerebellar signs in the reported observations of cerebellar abscess, the insufficient neurologic education of the otologist must be, in part at least, incriminated. Tests for passivity and disturbance of tonus are unknown to most otologists. These tests may be conducted even on a comatose patient and are signs of first rank in the semeiology of abscess of the cerebellum.

The vestibular syndrome is exhaustively discussed. Past pointing, nystagmus, Romberg's sign and vertigo are not purely cerebellar symptoms, but are due to disturbances in some portion of the vestibular apparatus. The discussion is epitomized as follows: "In the majority of cases of abscess of the cerebellum the vestibular syndrome embodies the characters of both peripheral and central vestibular lesions: peripheral in the deafness and areflexia, allied to the labyrinthitis, which so often has preceded the endocranial stage in cases of chronic otitis; central in the character of the spontaneous manifestations. These manifestations show that the syndrome is almost always in some manner and in some small part incomplete and inharmonious (Ramadier and Caussé). According to Barré, the lack of harmony is characteristic of cerebellar lesion and is not encountered in any other affection, but he does not consider it constant: A harmonious vestibular syndrome does not exclude the possibility of abscess of the cerebellum. Practically, two elements must be taken into account—both difficult to appreciate at times: (1) the progressive character of the phenomena and (2) the lability of the symptoms, that is, modification of the form and direction of the nystagmus and inversion of the past pointing."

Conjugate deviation of the eyes, paralysis of the ocular movements and lateral position of the head are regarded by some authors as an important syndrome.

Conjugate deviation of the eyes is seen most frequently; it is almost always toward the sound side and is a late symptom. Paralysis of the ocular movements is often associated with it. The significance of this syndrome is that in cases of abscess located elsewhere in the brain the deviation is different and is much more rare.

Troubles in respiration are frequent in cases of abscess of the cerebellum and are due to bulbar compression. Autopsy shows in all instances engagement of the cerebellar tonsils in the foramen magnum and dilatation of the ventricles. Paralysis of respiration may occur suddenly or after a long period of difficulty in respiration of the Cheyne-Stokes type. It may occur after lumbar puncture, which should always be performed with caution.

Paralysis of one or more cranial nerves in the course of abscess of the cerebellum is not exceptional. Although it is classic to regard paralysis of the third nerve as a localizing sign of cerebral abscess and paralysis of the sixth nerve as related to abscess of the cerebellum, reserve is advisable in interpreting their significance. They are not localizing signs of the first importance. It is a question whether in most cases of pyramidal disturbance there is not really instead a disturbance of tonus: massive hypotonia.

Statistics show that the diagnosis of abscess of the cerebellum is difficult. Five situations may be envisaged: (1) The syndrome of the posterior fossa is evident, but the difficulty lies in differentiating paradural abscess, collateral meningo-encephalitis and serous meningitis; (2) an encephalic abscess is evident, but the localizing signs of the abscess are absent, obscure or contradictory; (3) the abscess is masked by a complication (diffuse meningitis, thrombophlebitis, labyrinthitis and coma have their own signs, and these must not be confused with those of abscess); (4) there is a silent abscess, and (5) a patient with chronic otorrhea presents a nerve lesion such as tumor of the cerebellum, tumor of the angle or hysteria, which is independent of the otorrhea and, by reason of its location, has a symptomatology comparable with that of abscess. Differentiation of extradural, subdural and cerebellar abscess is not possible. Possibly, pain on percussion over the site of an extradural abscess may be of help. It has been said that the coexistence of a subdural abscess and a cerebellar abscess rarely occurs. Collateral meningo-encephalitis (hypertensive meningitis) may be generalized or localized in the posterior fossa (syndrome of Bárány). One of the most frequent etiologic factors in this condition is acute or chronic otitis. Hypertensive meningitis may exhibit all the aspects of abscess of the cerebellum, such as vestibular and cerebellar disturbances and affections of the cranial nerves. A preoperative differential diagnosis is not possible; even in cases in which a ponto-cerebellar lake is drained, the possibilty of the coexistence of an abscess remains. In the differential diagnosis of abscess of the cerebrum and abscess of the cerebellum, evidence obtained at an operation (mastoid exenteration, for instance) is valuable. The absence of precise signs or the presence of contradictory symptoms makes the diagnosis doubtful. Abscess of the cerebellum is often taken for abscess of the cerebrum.

Diffuse meningitis may mask the picture of abscess, not so much because it simulates abscess as because of the uncertainty of its significance. The problem will be solved by a study of the clinical and serologic data. In general, when signs of localization appear the diagnosis is already established, for in meningitis these signs appear late. The clinical picture of thrombophlebitis of the lateral sinus in its classic form is so characteristic and dominates the scene so completely that the observer's attention is directed away from a more profound examination. Likewise, it may be accompanied by neurologic signs, such as paralysis of the cranial nerves, papillary stasis and secondary meningitis, the clinical and cytologic characters of which are identical with those of meningitis secondary to abscess. It is to be remembered also that neurologic accidents may follow surgical intervention on the sinus. The possibility of the coexistence of acute labyrinthitis and abscess of the cerebellum is remote. In the presence of a vestibular syndrome, the differential diagnosis between a central and a peripheral lesion may be made on the basis of the evolution and arrangement of the symptoms. With a peripheral

lesion the onset is sudden and intense, and the symptoms tend to diminish rapidly after a few days, while with a central lesion the onset is insidious and the symptoms do not attain such intensity and tend to grow progressively worse. In labyrinthitis the syndrome is complete and in order, while in abscess of the cerebellum some elements are lacking and there is not harmony in the arrangement of the symptoms. Pure spontaneous vertical and rotatory nystagmus may be observed in cases of abscess but not in cases of labyrinthitis. Neumann's criterion that opening of the labyrinth is the touchstone for the differential diagnosis of labyrinthitis and abscess of the cerebellum is not accepted. In labyrinthitis headache, cytologic meningeal reaction, neurologic signs and stasis are absent, and the pulse rate is in relation to the temperature. If the labyrinth is nonreactive and labyrinthine symptoms then supervene, an endocranial complication is present. It is not uncommon for a patient with abscess to be presented in coma. In such cases the entourage must be interrogated, the ears examined and a caloric test made. In abscess of the cerebellum the coma is in reality stupor, and there will be some reaction on the part of the patient to examination. Also, examination for passivity and a lumbar puncture may be made. It is to be remembered that in profound coma the reaction to the caloric test is conjugate deviation of the eyes (the slow phase of nystagmus only). In a patient with otorrhea whose history cannot be obtained and who is in coma due to a cerebral cause, the lateralization of the neurologic signs in relation to the otorrhea often points the way to a correct diagnosis. In cases of doubtful diagnosis exploratory operation is indicated. Cases of silent abscess are exceptional. The only safeguard is for the otologist, who is treating the otorrhea, to examine the patient thoroughly at the first appearance of any untoward sign. The coexistence of otorrhea and an independent neurologic syndrome may lead to the false diagnosis of abscess of the brain or to overlooking of the latter condition. Tumor of the cerebellopontile angle may simulate abscess. Tuberculoma of the cerebellum, embolus of the posterior cerebellar artery, cerebellar hemorrhage and hemorrhagic pachymeningitis with cyst formation have been mistaken for abscess. Hysterical manifestations may, up to a certain point, simulate a cerebellar disturbance in a patient with otorrhea. The irritative point in these cases is constituted by a vertiginous episode, justified on an organic basis, the results of which are prolonged or exaggerated by hysteria.

It is recognized by the great majority of observers that the clinical signs do not permit an exact localization of the abscess in the cerebellum nor an estimation of its size. In fact, in the case either of abscess or of tumor, the edema accompanying the lesion contributes as much as the lesion itself to the clinical picture. It is impossible to dissociate that which belongs to the abscess from that which belongs to the edema.

It is not always possible to determine the pathway followed by the infection from the ear to the brain. At times the osseous lesions seem to be enclosed in healthy bone. In such cases it is believed that the organism follows vascular or perivascular pathways or that, in exceptional cases, the abscess may be metastatic. But in most cases the lesions of passage are discernible, either macroscopically or microscopically. In abscess of the cerebellum the infection travels to the retropetrous portion of the dura mater by preformed osseous or vascular pathways: the labyrinth, the petromastoid canal, emissary veins from the mastoid to the intracranial sinuses or, most frequently, directly by progressive osteitis. In the dura the infection may form an extradural abscess or pachymeningitis externa. In other cases there is a fistulous communication between the abscess and the dural lesion. Abscess of the endolymphatic sac is rare. Generally pachymeningitis interna is present, which solders the meningeal layers to the cortex of the brain and thus protects the subarachnoid space from infection. The infection is carried into the depths of the brain by vascular and perivascular pathways. The abscess almost always lies beneath the cortex on account of the arterial distribution. An avascular zone exists within the white substance, which is more vulnerable. While the cortex offers the maximum of resistance to infection, it is, how-

ever, more or less changed by lesions of congestive and edematous encephalitis. In more than half the cases the infection passes by way of the presinus zones, especially the labyrinthine; very rarely does the infection enter by the retrosinus route.

Abscess of the cerebellum is more frequently situated on the right side, and in two thirds of the cases it lies in the digastric lobule and the anterior part of the inferior semilunar lobule. Other locations are the vermis, cerebellar peduncles, pons and contralateral cerebellar hemisphere. The depth of the abscess is from 1 to 2 cm., and the volume is comparatively small. The bacteria are usually those observed in the otitic infection. Cocci tend to produce an encapsulated abscess and bacilli, especially the anaerobes, cause diffluent and encephalitic forms. Surrounding the abscess is a more or less extensive zone of encephalitis, accompanied by congestion and edema, thickening of the soft meninges and increase of the cerebrospinal fluid. The hypertension of the fluid may be aggravated by circulatory blockage at the level of the ventricles. The coexistence of hypertensive or cystic serous meningitis has been noted. Cerebral abscesses occur in four forms: (1) encapsulated, most common in abscess due to traumatism; (2) limited, in which the abscess is surrounded by a zone of encephalitis but not by a true capsule; (3) diffuse, in which the entire hemisphere may be involved in destructive encephalitis, often with numerous points of suppuration, and (4) diffuse encephalitis without suppuration.

The formation of pus is preceded by a stage of encephalitis: a small circumscribed zone, crowded with micro-organisms, leukocytes and disintegrated nerve elements, at the center of which is a thrombosed vessel. This stage is followed after a variable time by formation of pus and the establishment of defensive reactions. It would be clinically desirable to determine the time of transition between the two stages, since exploration in the first stage is particularly dangerous, but no clear indications are available. The abscess tends to extend centrally; the cortex resists invasion well. Left to itself, the abscess tends to open eventually into a ventricle or into the large meningeal spaces; exceptionally, it may open outward. When the abscess is opened and correctly drained, cure takes place by collapse of the walls and growth of granulation tissue. When this procedure is insufficient, as often happens in case of an encapsulated abscess, cure is retarded or doubtful. The acute abscess corresponds to the encephalitic and diffluent form, the subacute to the limited form and the chronic to the encapsulated form. The same etiologic and pathologic conditions associated with abscess of the brain may cause subdural abscess, which is usually situated near the osseous lesion.

The treatment of abscess of the brain of otitic origin comprises two stages: (1) the osseous stage, in which the otomastoid suppuration is eliminated and the dura laid bare, and (2) the meningo-encephalic stage—the treatment of the abscess itself. The classic procedure of puncture and drainage of the abscess seems best adapted to most conditions. Every cerebral abscess involves the immediate risk of death from meningitis or from compression of the bulb, especially abscess of the cerebellum. Hence, in principle, no delay is permissible in the institution of treatment after the diagnosis is made. In every case of suppurative otitis suspicion of an intracranial complication demands immediate ablation of the otitic focus and exploration of the adjacent dura.

Normally, the immediate effect of draining an abscess of the brain is marked amelioration of the symptoms. The nystagmus disappears after a few days; its persistence may be due to encephalitis or to a second abscess, and its reappearance points to poor drainage. Papilledema may persist for several weeks or months. Suppuration diminishes rapidly. In other cases the evolution is complicated by acute accidents supervening immediately after the operation, such as progressive aggravation of the condition, appearance of an encephalic hernia or sudden death. At times, after evacuation of the abscess signs of increased hypertension and papillary stasis appear. These may be due to hemorrhage in the brain substance and are to be combated by intravenous injections of hypertonic

saline solution and spinal puncture. In other cases rupture of a ventricle may occur. Persistence of symptoms is the result of poor drainage, encephalitis or the presence of a second abscess. If, in spite of adequate drainage there is no improvement, search for a second abscess is indicated. When a general infectious state, with rise of temperature and the appearance of hernia, is added to signs of hypertension, a severe encephalitic process must be suspected. Hernia is caused by the encephalitis, and the means of combating it consist of application of aseptic dressings under moderate pressure. Resection of the mass may be necessary.

Sudden death from bulbar respiratory syncope is almost always due to the presence of an unsuspected second abscess.

Next to generalized septic meningitis, abscess of the cerebellum is the gravest complication of suppurative otitis. The comparative figures for the incidence of cures of abscess of the cerebellum and abscess of the cerebrum are 16.66 per cent and 43.52 per cent, respectively. No one has approached the results obtained by Macewen in 1893. A surgical affection as variable in its form, structure and location as brain abscess cannot be amenable to but one operative method. To obtain the best results it is necessary to adapt the technic in each particular case.

DENNIS, San Diego, Calif.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, March 13, 1936

FREDERICK H. ALLEN, M.D., *President, in the Chair*

CONSTITUTIONAL FACTORS IN MENTAL DISEASE. DR. WALTER FREEMAN, Washington, D. C.

During the past ten years I have attempted to attack the problem of psychoses along four lines: anthropologic, nosologic, endocrine and chemical. My dominating idea has been that the constitution of the patient with mental disease—his biologic reactions, physique, susceptibility or resistance to disease, endocrine endowment and chemical peculiarities may yield pertinent information.

The constitutional and endocrine studies have been carried out on over 1,400 patients with psychoses. Since the problem was one of constitution rather than of etiology, the individual patients were separated into four types based on behavioristic or mental reactions, irrespective of age, sex or race and in actual disregard of the etiology of the disorder. In other words, a patient suffering from syphilis of the brain or arteriosclerosis but showing predominantly schizophrenic trends was placed in the group with schizoid disturbances. Other groups chosen included patients with paranoid, cycloid and epileptoid personalities. The validity of this sorting was checked in two ways. The death rate from tuberculosis and the weight of the heart were found to be almost identical in patients presenting true and those presenting symptomatic schizophrenia. Personality types other than these four were not sufficiently common in a psychiatric hospital for separate consideration.

Anthropologic studies based on the plan of Kretschmer showed a preponderance of patients of the asthenic type among the schizoid subjects, of the pyknic type among the cycloid subjects and of the dysplastic type among the epileptoid subjects, while the intermediate or athletic type was fairly well represented among the paranoid patients. Moreover, by photographing each body before necropsy it was found that the patients presenting a cyclothymic temperament were on the whole more agreeably and harmoniously proportioned than those of the other types; the parallel was drawn between the harmonious development of the cycloid personality and that of the body, and the peculiarity and disharmony of development seen so frequently in the epileptoid subject were pointed out.

In studying the susceptibilities and resistance to disease of the various psychiatric types, it was found that tuberculosis was overwhelmingly preponderant in patients of the schizoid group, that circulatory disasters seemed to occur more frequently in those of the cycloid group, that malignant disease and chronic streptococcic infection were common among paranoid subjects and that a persistent thymus and cerebral malformations were frequent in patients with epilepsy. On the other hand, diabetes was not found in persons of the epileptoid type, and malignant disease occurred only once; hernia was common among the cycloid subjects, but no cases of intestinal catastrophe occurred, and in studies used as a control based on deaths resulting from acute infections and deaths by violence there was a striking similarity in the ratios in each group.

Detailed study of the weight of the endocrine glands was taken up from two aspects—one a biometric study, under the direction of Dr. Raymond Pearl, with consideration of the pineal, pituitary, thyroid, parathyroid, thymus and adrenal glands and the gonads, with careful statistical handling of the material, and the other a simple separation of the subjects with the largest glands from those

with the smallest glands, with a comparison of the two groups for each of the endocrine organs. For instance, the 20 patients with the largest normal thyroid glands were compared with the 20 patients with the smallest normal thyroid glands in the whole necropsy material. It was observed in both studies that there was no correlation between the size of any of the glands and the type of mental reaction—cycloid, schizoid, paranoid or epileptoid. However, it was observed that subjects presenting exceptionally small pituitary, thyroid or adrenal glands or testes were often undifferentiated as to mental reaction, and from this it was argued that these endocrine glands supply something to the bodily economy, some energy component, that is necessary for the development and flowering of the personality.

A further instance of this was noted in an examination of the groups having large and small testes. In subjects having testes weighing less than 3.5 Gm. each, no instance of homosexuality was observed, whereas in persons with testes weighing 25 Gm. each an incidence of homosexuality of 10 per cent was found. It would seem that the testes provide the driving power necessary for the development of sexual interest, while something else controls the direction in which this interest leads. Furthermore, it was argued on clinical grounds that the endocrine system exerts a stabilizing influence on the personality, since the instability observed in hyperthyroidism, hypoparathyroidism, hypo-adrenia and hyperinsulinism were manifest. As far as determining whether a person will be proud, sensitive, suspicious and paranoid; timid, shut-in and dreamy; boisterous, jolly, hail fellow well met and cycloid, or moody, pedantic, egocentric and epileptoid the endocrine glands seem to have little to say.

The fourth line of attack was in the field of biochemistry. That the functioning of the brain is dependent on satisfactory conditions of oxidation, water balance, hydrogen ion concentration and salt equilibrium is well known, and some evidence was brought to bear indicating that dementia praecox may be associated with deficient oxidative processes in the cerebrum. The exhilaration produced by marked increase in barometric pressure was tested out by my colleagues and me before taking a patient with catatonia into the pressure chamber. The patient also became rather excited, talked only a little but scribbled furiously and ate a sandwich with relish, whereas previously he had been fed with a tube. Chemical tests on the cerebral cortex of a number of patients with dementia praecox revealed diminution of iron in the cortical ganglion cells. Other evidences of deficient oxidative processes in association with schizophrenia have been found by such investigators as Koch and Hoskins. In epilepsy there seems to be fairly definite evidence indicating a disturbance in water metabolism, although its exact nature is not yet known. From the chemical standpoint, as shown by Wuth, the economy of the person in a depressive stage of manic-depressive insanity resembles that of a hibernating mammal. The evidence for disturbance of colloidal dispersion in mental disorders is accumulating but has not yet reached a stage where it may be acted on successfully.

In summarizing the work, it seems that little more is to be gained from a study of the anthropologic, nosologic or pathologico-anatomic features of the body in persons suffering from mental disorders. Most studies on the endocrine system have been unsuccessful, but advances may be expected from the assay of the active endocrine principles in the circulating blood. The most promising lead seems to be in the biochemical field.

DISCUSSION

DR. CLIFFORD B. FARR: All are indebted to Dr. Freeman for bringing together within a relatively brief compass such a mass of facts, both positive and negative, bearing on the investigation of constitutional factors in mental disease. He has furnished a framework which few would have had the energy, talent and persistence to construct for themselves, into which one can fit isolated observations and give them a needed coherence. He may furnish one a fictional self-satisfaction that one had conceived it thus from the start. He finds a place for even the new

electrophysiology, in which some of my colleagues are actively interested at the moment. At various times in the last decade and a half I, frequently in association with my colleagues, have worked in the wide field which Dr. Freeman has described: basal metabolism in association with constitutional psychoses, anthropometry and personality studies, statistics on heredity, acid-base equilibrium and endocrinologic and other clinical studies. In all these fields our conclusions have been in substantial agreement with those voiced by Dr. Freeman. However, as regards his special domain of psychochemistry I choose to maintain a respectful, even an awed, silence.

Perhaps I can best complement, or supplement, Dr. Freeman's summary by some observations on physiognomy and emotional expression, topics on which he has lightly touched—deliberately, no doubt, for they are of relatively minor significance. None the less, physiognomy is largely determined by strictly constitutional factors, and relatively little by environmental or so-called conditional factors; of expression perhaps the converse is true.

The anthropometric aspects of physiognomy, as worked out by Draper, have been referred to by Dr. Freeman in his allusion to "the pernicious anemia race," "the poliomyelitis race," etc., in discussing constitutional susceptibility to disease. It need not, therefore, be considered further.

Dr. William King Gregory, of the American Museum of Natural History, in his fascinating book entitled "Our Face from Shark to Man," has pointed out that the basic facial "patents," as he aptly calls them, derive all along the evolutionary line from the lowly shark to Homo sapiens and are, therefore, in the strictest sense constitutional. Nevertheless, as orthodontists have demonstrated, human features are subject to wide deviations as the result of conditioning factors and can be artificially restored. Darwin, in his famous book "Expression of the Emotions in Man and Animals," similarly showed that "emotional expressions are survivals of movements that were once useful in the animal series, when in the presence of conditions which excited the emotion." In persons suffering from mental illness one frequently sees expressions which are clearly regressions to these more primitive manifestations. On the other hand, modern biologists have enunciated principles which explain changes in expression and physiognomy as conditioned. I quote the statement of an anonymous writer in the "Encyclopaedia Britannica," (ed. 14, vol. 17, p. 887): "Muscles concerned in producing skin fo'ds become strengthened by habitual action, and when the skin diminishes in elasticity and fulness with advancing age, the wrinkles at right angles to the course of the muscular fibers become permanent. . . . Action of this kind may, by affecting local nutrition, alter the contour" of related bones and cartilages. But even this principle may be interpreted conversely and bring back the constitutional factor. I quote a statement by the same writer: "If the mental disposition and proneness to action are inherited by children from their parents, it may be that the facility in and disposition towards certain forms of expression are in like manner matters of heredity" and are hence, I may add, constitutional.

Finally, I wish to touch briefly on another, but related, topic, alluded to by Kretschmer in his book (Körperbau und Charakter, ed. 9-10, Berlin, Julius Springer, 1931) but more fully discussed by Hellpach (*Med. Welt.* **7**:1546, 1933). Dr. Hellpach considered the formation of the face on a racial basis. He described and analyzed typical facial expressions for the different Teutonic strains in Germany: the upper and lower Saxons, the Westphalians, the Franks, the Schwabians and the Bavarians, the general distribution of these peoples corresponding roughly to the new division of the reich proposed by Hitler. These racial strains all have characteristic variations of facial expression which Hellpach ascribed in part to differences in dialect. The habitual use of certain facial muscles to express these variable sounds induces specialized muscular development, in accordance with one of the principles already quoted. After describing the features of these modern representatives of old German tribes, he said: "The formation of the face is completely explained by the demeanor and manner of speech." He also took into account other factors, such as heredity, constitution,

climate, etc. He then stated that these German strains have, nevertheless, facial expressions in common, which completely distinguish them from people living east of a meridian running from Trieste, Italy, in a northeasterly direction. (This line is really that of the Polish Corridor.) In this country it might be possible to find similar groups of people of common English ancestry, but with distinctive manners of speech, social customs and outlook on life and subjected to differing climatic and environmental conditions, who manifest equally characteristic facial expressions; for example, certain isolated communities in New England and the South. In the same connection, I have frequently been struck by the characteristic racial expression of Scandinavian immigrants (actually, first cousins of the English race) and the complete lack of any such expression in their American-born and American-educated children or grandchildren. Here again, the hypothesis of language differences and habitual mental trends may be considered to be operative. Also, the same general principles explain the "serene" (or troubled) expressions of "age." In the latter connection there may again be recalled the production of folds by the principle of habitual muscular action. Walt Whitman probably had this in mind when he said of women: "The young are beautiful; the old are more beautiful."

DR. JOHN CHORNYAK: Dr. Freeman, in this interesting and comprehensive paper, has discussed what he calls "psychochemistry," especially in relation to oxidation and the inadequacy of the iron (a catalyst in oxidation) in cases of schizophrenia. On the basis of extensive experimental work on asphyxia, my colleagues and I have shown that the neurons in the same brain do not have the same metabolic rate. The neurons in the supragranular lamina of the so-called psychoprojection or associational areas are the most vulnerable to deprivation of oxygen. The sensory cells and the cells of the correlation centers are more susceptible or vulnerable to oxygen deprivation than are neurons of the large polygonal motor type (Malone). This situation is the reverse of that in the rat and illustrates the danger of applying the results of cortical extirpation in the rat (Lashley) to conditions in higher forms. These effects are conditioned by the fact that decreased oxidation acts primarily as a stimulating agent (Loevenhart and others). The effects of oxygen deprivation on the circulation are profound, but a description of these vascular lesions is not directly applicable to the point made by Dr. Freeman and will therefore not be discussed.

The psychologic effects on human behavior of atmospheres deficient in oxygen has been well investigated as a result of the needs of modern aviation. A review of all this literature, with the results of his own extensive research on the subject, is found in McFarland's monograph (*Arch. Psychol.*, 1932, no. 145).

This investigator stated that at a certain level of oxygen deprivation there is a stimulating effect on the psyche. In atmospheres deficient in oxygen, reactions of choice are the first to be affected and then the less complex sensorimotor acts. This writer cited the interesting observation that aviators like best to fly at the level of about 14,000 feet (5,267 meters). In this percentage of atmospheric oxygen they can pay much better attention to the instrument board. The drawback, however, is that their judgment is impaired.

This phenomenon raises many interesting problems and questions with reference to schizophrenia, in which Dr. Freeman has demonstrated a deficiency of the oxidation catalyst iron. Does this account for the so-called brilliant person in whom a schizophrenic psychosis develops at adolescence? Is this precocious brilliancy due to the fact that at a certain level of decreased oxidation these persons were able to pay better attention to scholastic duties? How frequently is there a history in these cases of acts showing poor or bad judgment? My experience in psychiatric practice is too limited to give any dogmatic answers to these questions. However, in a few cases of schizophrenia with a history of "precocious brilliancy" one could ascribe the good scholastic results based on good attention to this state, whereas in the same person there were acts of behavior that showed a marked lack of judgment, if they were not actually schizoid in quality.

The question of what Dr. Freeman calls psychochemical changes, especially the oxidation-reduction phenomena in the central nervous system, is of great importance for psychiatry and, more specifically, for an understanding of hysteria and schizophrenia.

The physiologic characteristics of the personality types and the types of persons who are susceptible to mental illnesses have been studied by the method of conditioned reflexology by Pavlov in dogs and by Krasnogorski in children. Briefly, Pavlov's work has shown the following four groups (with all gradations between the extremes): First, the type of nervous system in which the process of excitation predominates and inhibitory reflexes are established with great difficulty and when formed are readily disinhibited, being very unstable. This type Pavlov considered to correspond to the human subject in whom neurasthenia, hypomania or manic-depressive psychosis develops. Experimental neurosis is readily produced in such dogs by forcing a conflict between these two processes of excitation and inhibition. There are two types of the balanced temperament in which either the excitatory or the inhibitory reflexes can easily be formed. The balance of these two fundamental processes is normal. Objectively, there are in animals of this balanced type two externally different reactions. Animals with the one are lively and make friends readily; those with the other are quiet and undemonstrative but represent, nevertheless, a powerful and balanced type. An experimental neurosis cannot be produced in such animals. They are considered to correspond to the majority of persons, who do not succumb to mental illness, despite many psychic and toxic traumas. At the other extreme is the highly inhibited type, in which excitatory reflexes are established only with marked difficulty and when formed are easily inhibited. The inhibitory process is evidently a protective mechanism to prevent fatal exhaustion of a defective cerebrum. Experimental neurosis is easily produced through a conflict between excitatory and inhibitory reflexes or through a strong and unusual stimulus. This type corresponds to human beings who present the inhibitory diseases, such as psychasthenia, hysteria and schizophrenia.

Krasnogorski demonstrated the same types in children. He extended this analysis, however, by differentiating the types as to whether the normality or the weakness is cortical or subcortical or both.

True Hermaphrodism: Report of an Unusual Case. Dr. Ralph C. Kell, Dr. Robert A. Matthews and Dr. Albert A. Bockman (by invitation).

This paper will be published in full later.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, March 19, 1936

S. W. Ranson, M.D., *President, in the Chair*

Evidence of Altered Carbohydrate Metabolism in Cats with Hypothalamic Lesions. Dr. W. R. Ingram and Dr. R. W. Barris (by invitation).

The blood sugar was estimated in 55 cats after the production of lesions in various parts of the hypothalamus. Forty-two showed postoperative hyperglycemia, which was always transient and, provided the animal survived, returned to normal or subnormal levels. Seven cats showed no abnormality in the blood sugar level at any time after the operation. Ten showed a tendency to mild, frequently intermittent, chronic hypoglycemia—some of these showed transient hyperglycemia in the early postoperative period. Analysis indicates that, so far as groups of animals are concerned, transient hyperglycemia may occur after the production of lesions at almost any point in the hypothalamus. On the other hand, hypoglycemia is

most frequent when the lesions are in the anterior portion of the hypothalamus, and in the majority of these instances the nucleus filiformis is destroyed or atrophic. There may be individual exceptions, however.

Nine cats with bilateral lesions in the anterior, suprachiasmic portion of the hypothalamus but with no direct damage to the hypophysis, showed increased sensitivity to insulin as compared with normal cats used as controls. In these animals there was some degree of injury or atrophy of the filiform nucleus on both sides, although the participation of this structure in carbohydrate metabolism is not definitely proved. Five other cats with lesions in the hypothalamus which did not affect this region so extensively showed normal responses to insulin.

Five cats with severe damage of the hypothalamus in the suprachiasmic region showed a diminished response of the blood sugar to epinephrine.

Four of 5 cats with lesions in the suprachiasmic region failed to show normal responses to the hyperglycemic effect of a suspension of anterior pituitary which was effective in normal cats. Three hypophysectomized cats showed retarded responses to the action of this preparation, but the results are not directly comparable, since the dose of anterior lobe was much less than that in the 5 cats already mentioned.

The glycogen content of the liver, determined just before the animals were killed, was normal in all cats except one without a hypophysis, which had been under starvation conditions for several days.

In a cat with bilateral hypothalamic lesions but no direct injury to the hypophysis, there were repeated hypoglycemic crises, which could be prevented by treatment with a preparation of anterior lobe. There were considerable damage of the anterior portion of the hypothalamus and tuber cinereum and marked widening of the third ventricle, which apparently was due to atrophy of its walls.

Whether the disturbance in carbohydrate metabolism is due to a direct effect of the nervous lesions on visceral structures or to an effect on the hypophysis has not been determined.

DISCUSSION

DR. S. W. RANSON: I wish to ask whether there was any relationship between the height of the hyperglycemia and the location of the lesion. Apparently, there was hyperglycemia in about the same number of instances whether the lesion was in the anterior, posterior or middle portion of the hypothalamus. Was there any difference in the height of the hyperglycemia?

DR. W. R. INGRAM: There was no noticeable difference. Perhaps a corresponding number in each group showed hyperglycemia.

DR. PERCIVAL BAILEY: I presume that if the lesion in the hypothalamus causes involvement of the hypophysis it would have to be through the sympathetic nervous system. I wish to ask Dr. Ingram whether he has tried sectioning the cervical portion of the sympathetic trunk before injuring the hypothalamus.

DR. INGRAM: We have not tried that. I do not know whether or not Dr. Davis or Dr. Cleveland has done so. Perhaps Dr. Davis could say.

DR. LOYAL DAVIS: We have removed the cervical sympathetic ganglia and cervical portion of the trunk but have not been able to influence the hyperglycemia and glycosuria produced by removal of the pancreas; neither have these procedures had any effect on the influence of a hypothalamic lesion in such pancreatectomized animals.

DR. VICTOR E. GONDA: I wish to know what effect was produced on the temperature.

DR. W. R. INGRAM: The temperatures were not studied carefully in these animals, except in the early stages to determine the condition of the animal after operation. Other experiments on temperature regulation are now being carried on in the laboratory by Dr. Ranson and others.

After a course of treatment with anterior lobe, which elevated the blood sugar, discontinuing administration of this substance caused a pronounced drop in the blood sugar content to as low as from 45 to 50 mg. per hundred cubic centimeters.

DR. S. W. RANSON: In regard to the effect on the temperature, my associates and I have found that in animals with lesions in the anterior portion of the hypothalamus there was a tendency to temperatures above normal for a few days or a week. These animals maintained their heat well against cold in a room with a temperature around 0 F. There was some indication that they do not combat high temperatures as well.

GALVANIC FALLING IN CLINICAL USE. DR. EDWIN J. BLONDER (by invitation).

This article is published in full in this issue, page 137.

TREATMENT FOR CHOREA MINOR BY MEANS OF ELECTROPYREXIA. DR. MAURICE L. BLATT, DR. CLARENCE A. NEYMANN and DR. S. L. OSBORNE.

The treatment for Sydenham's chorea has always been symptomatic. The disease has been recognized as self limiting, disappearing in from two to six months. Most physicians have considered it as belonging in the group of rheumatic diseases. In 1929 Roeder treated a patient with phenyl-ethyl-hydantoin. After the typical sickness from this drug improvement was noted, and a number of other observers substantiated Roeder's observation. Sutton, Dodge and Bateman used typhoid vaccine for the purpose of producing therapeutic fever in patients with chorea and reported excellent results.

We expressed the belief that electropyrexia was indicated in the treatment for chorea shortly after Neymann and Osborne introduced this therapy. However, it was not until August 1934, when electromagnetic induction by means of high frequency current was introduced, that electrotherapeutic fever became practical as a treatment for chorea. Neymann made a preliminary report on the first 7 patients studied in 1935, since which 13 more children with chorea have been treated.

Of the 20 cases in this series, the disease was very severe in 7, moderately severe in 5 and comparatively mild in 8. The average period of hospitalization was less than sixteen days, and the average number of treatments less than four. One child remained in the hospital thirty-nine days and had ten biweekly treatments. The shortest period of hospitalization was five days, with two treatments.

The patients have been under observation for from five to twenty months since discharge from the hospital. There have been recurrences in 2 children, in 1 of whom the disease apparently was not of a rheumatic type but was probably nonsuppurative encephalitis. The other 18 children remained well.

In view of the frequency of acute carditis in this disease, great care must be taken in the treatment of patients showing this complication. The first session of therapy in such cases should be shorter and the temperature peak lower than in cases of uncomplicated chorea.

As a rule, the temperature is raised to 39.7 C. (103.5 F) as rapidly as possible and maintained between this point and 40.6 C. (105 F.) for about eight hours. Temperatures above 105 F. endanger the child because of the possibility of producing convulsive seizures, during which the temperature rises still higher.

The electromagnetic induction used is dependent on a current oscillating at the rate of 30,000,000 cycles a second. The current is led through a flexible cable placed outside a nonconductive sleeping-bag. This insulation is necessary in order to protect against burns. An air-conditioned cabinet may be used instead of this treatment bag, but in the handling of children the bag has proved satisfactory. It is essential that the patient be constantly watched by the physician and nurse during treatment to avoid the danger of hyperpyrexia and to prevent, as far as possible, the discomfort attendant on eight hours with a temperature of 105 F. During treatment the patient is given fruit juices and a 0.6 per cent saline solution to replace lost fluid and sodium chloride.

1. Twenty children with chorea were treated with artificial fever produced by electromagnetic induction.

2. In all cases the choreiform movements ceased promptly.

3. The average period of treatment and hospitalization was sixteen days; an average of four treatments were given each patient.

4. Chorea recurred in 2 children.

5. Electropyrexia is not contraindicated in cases of rheumatic carditis complicating chorea.

6. In contrast to devices dependent on external heat, magnetic induction seems to us to be a superior method for producing therapeutic hyperpyrexia.

DISCUSSION

DR. ARTHUR WEIL: I wish to know on what theoretical premises the authors founded this method of treatment for Sydenham's chorea. From what has been said it seems that they still accept the theory, now mostly abandoned, that this type of chorea is always encephalitis in connection with rheumatism. Did the authors assume then that they were dealing with a form of chronic encephalitis which could be influenced by hyperpyrexia in a way similar to that in syphilitic polio-encephalitis associated with dementia paralytica? Most modern writers on Sydenham's chorea agree on one point, namely, that one is concerned in this disease merely with a complex of symptoms of manifold etiology. It appears from the table which was presented that in only about 5 cases of the series was rheumatic endocarditis definitely present; besides, there was 1 case of hemichorea. The practical significance of the results obtained must, of course, be decided by the clinician and not by theoretical argumentation about the etiology of the disease.

DR. FRANCIS J. GERTY: What results were secured with other choreiform types, such as Huntington's chorea?

DR. BENJAMIN BOSHES: Were any sedatives used in these cases?

DR. R. P. MACKAY: I wish to ask what justification there is for subjecting patients with a disease which has a tendency to cardiac involvement to such a physiologic earthquake as this treatment involves. There is a fundamental difference between the physiologic behavior of fever produced by the use of foreign proteins and that produced by physical means. When one subjects a patient to heat by physical agents the physiologic effects are about as follows: There is first an attempt to eliminate heat by increased sweating, a process which involves loss of water and chlorides. When this proves inadequate, the peripheral vessels of the skin dilate in order to radiate heat. This leads to a fall in the diastolic blood pressure and an increase in the pulse rate, with a greater burden on the myocardium. When both evaporation and radiation prove inadequate, the respiratory rate rises, further increasing the loss of water and also blowing off carbon dioxide and producing relative alkalosis, sometimes with tetaniform manifestations. When all these mechanisms fail the temperature of the body rises.

One must admit that this method involves a tremendous physiologic strain, which might contraindicate its use for patients with Sydenham's chorea.

On the other hand, after the injection of a foreign protein into the body, the first concern of the heat-regulating mechanism is to produce and conserve heat. In the phase of chill muscular contraction increases heat production, while sweating is reduced and the peripheral vascular tree undergoes constriction, thus diminishing elimination of heat. As a result, the body temperature rises. This process does not involve a loss of large amounts of water and chlorides or a fall in blood pressure and extra strain on the myocardium.

If it is true that the fever produced by typhoid vaccine is adequate in the treatment for chorea, what is the advantage of using a method which so penalizes the patient and is expensive, cumbersome and difficult to manage?

DR. MAURICE L. BLATT: I wish to thank the discussionists for the points raised, for they are problems to be considered definitely in treatment of this type.

I can work forward in this way: In comparatively few cases of chorea is autopsy performed, for few children die during the acute stage of the disease. We have little definite knowledge of the essential histopathologic changes in the

brain. We have seen many children die later of acute rheumatic carditis. Death does not occur during the first attack but more often after subsequent severe rheumatic complications. The conception that chorea is of rheumatic origin is just as difficult to substantiate as is the etiology of rheumatism. These diseases frequently begin with tonsillitis or pharyngitis, as do many infections of childhood. Rheumatic manifestations rarely occur until after the third year of life. They frequently begin as muscular pain. The "growing pain," or "hip pains" that awaken the child at night are, in our opinion, of rheumatic origin. Because chorea, carditis, multiple arthritis and muscular pain are frequently associated in one combination or another, they are classified as rheumatic. In bacteriologic studies of chorea repeated cultures have been made, and occasionally a diplococcus has been obtained. At a later date, however, endocarditis has developed, and the results have been considered questionable because of the complication. Blood cultures have been made by many observers in the hope that an organism might be obtained, but there has been no agreement as to the organisms recovered.

The pathologic observation in the brains of the few children on whom autopsy has been performed was encephalitis. We believed that 1 of the children we treated had not Syndenham's chorea but some other type of encephalitis. In our experience mental deterioration and personality changes are extremely uncommon in cases of Sydenham's chorea; they occurred in this child.

I think Dr. Mackay's position is well taken, but there are extenuating circumstances for this treatment. If one can prevent the recurrence of chorea by this method one will prevent crippling carditis. It is not only the first attack but subsequent attacks that affect the heart. These patients were carefully observed. Dr. Neymann remained with them during the treatment, and the patient was adequately attended by residents and nurses, so that at no time during treatment was the patient in danger. In 1 case in which hemoglobin and blood cells appeared in the urine, we waited to see whether the urine would clear before repeating the treatment. It did, and we repeated the treatment. The urine again showed blood but promptly cleared.

No sedatives or other drugs were used in the cases described in our series. The patients were kept in bed and were given a normal ward diet. They received nothing that would interfere with the observation of the effect of the new treatment.

There is an economic element in connection with the treatment of chorea. It is desirable to shorten the number of hospital days. We think it worth while to attempt this. In the past our patients have been hospitalized for from six weeks to three months or confined to their homes for a like period. This is a great strain on an institution and a family. If one can discharge a patient in two or three weeks one saves the family expense. If hospital beds are filled with patients with rheumatic-myocardial infections which might have been avoided by this treatment, the treatment is justified. We have demonstrated that this method can be used to good advantage without harming the patient. We shortened the number of hospital days.

Four or five years ago we tried typhoid vaccine. We were able to produce fever, but the curative results in our series were negligible. We did not think that we had shortened the course of the disease. I am without experience in the use of other foreign proteins in this disease.

DR. CLARENCE A. NEYMANN: Several years ago 2 patients with Huntington's chorea were treated with artificial fever. From the lack of response to this therapy in these cases, we concluded that electropyrexia is not indicated in this disease.

In reply to Dr. Mackay, I wish to call his attention to the fact that Sutton first used typhoid vaccine in treatment for Sydenham's chorea in 1931 (Sutton, L. P.: Treatment of Chorea by Induction of Fever: Preliminary Report, *J. A. M. A.* **97**:299 [Aug. 1] 1931). Later, another group of patients was treated by Sutton and Dodge. Their results were not nearly as good as ours, and they reported 1 death as a direct result of the treatment. According to Dr. Mackay, who has discussed electropyrexia on other occasions, one might be led to believe

that whenever this therapy is used death is to be expected. These chimerical deaths are supposed to be due to the tremendous strain on the cardiovascular system. Besides, Dr. Mackay seems to imply that the treatment is so severe that it can hardly be borne. Aside from these children with chorea, I have treated over 500 patients suffering from dementia paralytica, tabes dorsalis, multiple sclerosis, rheumatism, gonorrhea and primary and secondary syphilis. In this entire series 2 deaths occurred. These deaths might have been avoided if I had been better versed in the contraindications of treatment. One death occurred in a case of multiple sclerosis, in the final stage of the disease, and the other was the result of treating a patient with dementia paralytica who, having previously been subject to convulsions, entered a continuous convulsive status when his temperature reached 106 F. The death rate is, therefore, negligible.

When we began to treat chorea we were determined not to risk death or permanent injury to the heart. In this series, the children with rheumatic carditis, far from experiencing a permanent heart injury, improved beyond our expectations. We have not discussed the disappearance of heart murmurs and other cardiac symptoms, for we realize that these are subjective observations. The electrocardiograms taken before and after treatment demonstrate objective findings. Two cardiologists would hardly believe that the electrocardiograms had been obtained from the same patient before and after treatment. The alleged danger to the cardiovascular system is grossly overrated. It is frequently present in the minds of physicians whose experience with electropyrexia is purely theoretical.

Regular Meeting, April 16, 1936

S. W. Ranson, M.D., *President, Presiding*

Surgical Treatment of Migraine. Dr. Eric Oldberg.

(A preliminary report was made of the cases of 5 patients on whom the middle meningeal artery has been divided for relief of the headache of migraine.)

DISCUSSION

Dr. Meyer Solomon: What are the clinical effects of dividing the middle meningeal artery in any patient, either on one or on both sides?

Dr. Victor E. Gonda: Would not periarterial stripping do, instead of sacrificing the vessel?

Dr. Paul C. Bucy: Has Dr. Oldberg investigated the results of section of the middle meningeal artery and retrogasserian neurectomy in patients suffering from both trigeminal neuralgia and migraine? If the reported observations are correct, this procedure should relieve such patients of both these painful disabilities.

Dr. Eric Oldberg: The only way one would be able to demonstrate the effect of dividing the artery would be to expose the artery by making a bone flap, to see that no blood passed through it. I do not see any need for periarterial stripping. It is much easier to clip the artery.

In reply to Dr. Bucy's question: I have not made such an investigation, but I think it would be a good plan to inject alcohol into the third division of the nerve in some cases; if the trigeminal fibers transmit the pain that procedure should cure the migraine. It should also stop the headache if the pain is transmitted by fibers from the otic ganglion, since these also enter the skull by way of the foramen ovale. It would be interesting to see if histamine headache could be stopped by injection of the third division of the trigeminal nerve.

FACTORS INFLUENCING BRAIN POTENTIALS. DR. R. W. GERARD (by invitation).

Nerve cells may manifest spontaneous rhythmic activity. This is influenced by impinging nerve impulses and, more constantly, by the physicochemical condition of the neuron and its bathing fluids. A study of some of these controlling factors is reported in this paper.

Spontaneous rhythms and optic responses of the cat's cortex and lateral geniculate body were recorded with the cathode ray oscillograph (concentric needle lead and Horsley-Clarke instrument). Human records with the scalp intact were taken with plate leads.

Cortical rhythms and responses were reversibly abolished by local application of isotonic solutions of potassium chloride or calcium chloride, although Ca^{++} first antagonizes K^{+}. Weaker concentrations of K^{+} given intravascularly increased motor activity, prolonged after-discharges and exaggerated the fast rhythm and optic response of the geniculate body. Spikes were often inverted. Ca^{++} depressed activity, after-discharges and fast waves. Citrate acted like K^{+}. Strong concentrations of carbon dioxide depressed and slowed rhythms; weaker concentrations (such as that produced in the human subject by holding the breath) decreased or disrupted the 10 a second waves but strongly increased the 40 a second waves. Hyperventilation augmented the fast waves. Polarization with constant currents increased rhythms, especially the faster ones, with little effect on the optic responses in the cat. Feebler currents (in the human subject) rather decreased rhythms. Thyroid feeding accelerated both fast and slow rhythms (in 1 human subject).

In light normal and hypnotic sleep the rhythm of 10 waves a second increased in size and regularity; in stages of deep sleep activity disappeared, and a rate of 14 waves a second was observed at some stages in both normal and hypnotic sleep. Rhythms can sometimes be affected by suggested stimuli (in hypnosis), as by the actual ones. Several unique wave patterns were recorded in early stages of schizophrenia.

SPINAL EXTRADURAL CYSTS. DR. RALPH B. CLOWARD (by invitation).

Nonparasitic extradural spinal cysts are rare. Up to the present only 9 cases of such cysts have been reported in the literature: 1 by Schlesinger, in 1898; 1 by Krause, in 1908; 1 by Mixter, in 1932; 4 by Elsberg, Dyke and Brewer, in 1934, and 2 by Lehman, in 1935. The following case may be added to this list:

A man aged 43 entered the Albert Merritt Billings Hospital on April 2, 1935, complaining of weakness of both lower extremities for two years and mild pains in the thighs for four months. Examination gave negative results except that the lower extremities showed atrophy of the muscles of the thigh, muscular fibrillations, mild spasticity and a positive Babinski sign on the right. There were sensory loss over the twelfth thoracic dermatome and reduction of sensation below this level. Spinal puncture revealed no block. The cerebrospinal fluid was normal. Roentgenograms of the spine demonstrated a large, expanding intraspinal lesion, the spinal canal being from 2 to 15 mm. wider than normal at the twelfth thoracic and the first and second lumbar segments.

At operation, performed by Dr. Percival Bailey on April 28, a large cyst extending from the eleventh dorsal to the fourth lumbar vertebrae was easily dissected from the dura mater and laminae. Examination of the cyst revealed a thin-walled sac, measuring 14 by 5 by 4 cm., filled with colorless fluid. The wall was composed of an acellular fibrous connective tissue, with a definite single layer of flat cells lining the inner surface.

The interesting findings in this case not recorded in others of the kind were: The patient was an adult; the cyst was located in the lumbar region, and the cerebrospinal fluid and results of the manometric test were normal, in spite of the enormous size of the tumor. All cases previously reported have been those in adolescents; the tumors were all located in the midthoracic region, i. e., between the fourth and the tenth thoracic vertebra, and a manometric test demonstrated a subarachnoid block, with characteristic changes in the spinal fluid.

DISCUSSION

DR. HAROLD C. VORIS: Does not Dr. Cloward think that there is a possibility that when the spinal puncture was performed the needle, instead of entering the subarachnoid space, may have invaded the cystic sac and that the manometric readings were obtained as the result of the spinal fluid pressure being transmitted to the cyst. It seems to me that with the position of the cyst this conclusion is possible.

DR. MEYER SOLOMON: In referring to the absence of block did Dr. Cloward include partial block, by which I mean one indicated by a delayed rise, a delayed fall, a slow rise, a slow fall, a new level or a reduction of the pressure to approximately zero on removal of about 7 cc. of spinal fluid, or any combination of these.

DR. R. B. CLOWARD: At operation the largest part of the sac was at the first lumbar vertebra, where it completely filled the canal. From there it tapered to a pointed lower end at the fourth lumbar vertebra. The spinal puncture was made at the usual level, between the third and the fourth lumbar vertebra, and there the sac was relatively small. It may have been possible for the spinal puncture needle to enter the cyst, but the fact that the iodized poppy-seed oil which was injected at that time was seen with the fluoroscope to pass above and below the lesion proved definitely that it did not.

There could have been no partial obstruction, for there was no delayed rise. The fluid rose and fell rapidly in the manometer when pressure was made on the jugular veins.

DR. PERCIVAL BAILEY: I should mention that the iodized poppy-seed oil was injected at the time when the Queckenstedt test was made and that it passed to the bottom of the sacral sac and high into the thoracic region, which is evidence that the needle was not in the sac. The response to the manometric test was normal, and the fluid rose and fell quickly.

DR. MEYER SOLOMON: Popper and Hurxthal (Normal Cerebrospinal Fluid Dynamics in Spinal Cord Tumor Suspects, *J. A. M. A.* **103**:391-393 [Aug. 11] 1934), as the result of experimental work with an artificial spinal canal, came to the conclusion that as long as an opening as large as the bore of the lumbar puncture needle remains the entire length of the canal no changes from the normal hydrodynamics, not even partial block, should be expected, if the character of the wall, the viscosity of the fluid and the size of the opening remain constant.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 27, 1936

FREDERIC H. LEAVITT, M.D., *President, in the Chair*

CASE OF TRAUMATIC PSYCHOSIS IN A CHILD. DR. J. C. YASKIN and DR. GEORGE WILSON.

Mental retardation and personality and behavior disturbances resulting from cranial trauma are relatively common and have received considerable attention in the literature (Healy, William: The Individual Delinquent, Boston, Little, Brown & Company, 1915; Kasanin, J.: Personality Changes in Children Following Cerebral Trauma, *J. Nerv. & Ment. Dis.* **69**:385, 1929). Major psychoses of childhood resulting from trauma affecting the cranium or other parts of the body are rare and have received little attention in the literature. The occurrence of a major psychotic reaction following a relatively slight trauma prompted the report of this case.

History.—J. W., a boy, when first examined on March 5, 1934, was 9 years of age. He was the fourth of 5 living children, was born at full term by a normal

delivery, walked and talked before the age of 1 year and gained control of the sphincters before the age of 18 months. He entered kindergarten at the age of 5 and completed two classes of grammar school in June 1932. He made excellent progress in school, was a good mixer and behaved well. He had had no serious illness, injury or operation. The family history revealed that 1 sibling was feebleminded and died at the age of 5 years.

On Sept. 12, 1932, while he was playing, his coaster-wagon was overturned by a horse; the boy rolled over, struck his head on the sidewalk and injured his left ankle. When taken to a physician's office he appeared dazed, and examination revealed a hematoma on the head and some injury to the left ankle. Roentgenographic studies later revealed a fracture of the astragalus. Within a few weeks after the injury decided changes in personality appeared. At first he was irritable and unkind. Later he became uncooperative, disobedient and aggressive. Within a few weeks he stopped using articulate language, appeared to take no cognizance of the surroundings and spent his time lying in one position, the arm flexed at the elbow and the fists clinched and pressed tightly against the face and teeth. The legs were sometimes flexed but were usually extended. As speech and interest in the surroundings were lost, he began to emit wild noises reminiscent of an angry cat. He kicked, struck or bit any one approaching him; sometimes he kicked without reason and fell off the bed. When hungry or thirsty he made his wants known by shrieking. Within a few months it became impossible to feed him in the usual way, as he had a tendency to bite and chew glass. When food neared his mouth he grabbed it with his fists, rubbed it against his mouth and spilled it around him. He usually defecated and urinated wherever he happened to be, although sometimes he denoted his wants by shrieking. He slept poorly and usually was noisier at night than in the daytime. He recognized no one in the family, paid no attention to commands and was hostile.

Examination.—The boy lay on his right side, with the head flexed, the fists clenched and buried in his face and the legs extended. When the father attempted to approach, the child shrieked and kicked violently. While thin, he was not profoundly emaciated or pale. The heart sounds appeared normal; no masses were felt in the abdomen; there was no glandular enlargement in the neck, and the teeth were widely spaced. The throat could not be examined.

There was a definite cracked pot sound, more marked on the left side of the head than on the right. There was no rigidity of the neck. One could not state with certainty that the patient could see; he kept the eyes tightly closed. When the eyes were forcibly opened they moved freely in all directions; the pupils were moderately dilated and responded to stimulation with light. The facial musculature appeared to be equally innervated on both sides. One could not be certain that the boy could hear. The pupils were rapidly dilated by instillation of a 5 per cent solution of cocaine; after considerable struggling the fundi were seen. They appeared somewhat pale, but there was no evidence of a "cherry" spot, edema or hemorrhage.

There was no weakness in the upper or lower extremities; in fact, it required a blanket and both the father and brother to restrain the patient. The biceps and triceps jerks were active bilaterally. The abdominal reflexes could not be obtained; the knee and achilles jerks were active bilaterally, and there was a spontaneous Babinski sign on the right. The results of plantar irritation could not be gaged accurately, as the patient drew the limbs away violently. No atrophy was noted in any part of the body; superficial and deep sensibility could not be estimated accurately, as attempts at stimulation resulted in violent kicking. When it was attempted to make the boy walk he hung on to the person assisting him, dragged his feet, screamed and kicked.

A roentgenogram of the skull taken shortly after the accident revealed no evidences of fracture or other abnormalities. The Wassermann reaction of the blood was negative.

Course.—The patient was reexamined on Sept. 27, 1934. The parents stated that in some respects he was better; he did not kick, scratch or bite as he had

a year before and was therefore, somewhat easier to manage. In other respects the condition was essentially unchanged. He slept from four to five hours a day, usually on his face and abdomen, with his hands at his mouth. When placed on the toilet at regular intervals he voided and defecated, but when left alone he had involuntary movements. When fed at regular intervals he took food hurriedly and swallowed it without chewing. He did not utter sounds and never made demands by gestures.

The boy was found sitting in the kitchen, with his eyes closed and the head bent forward, chewing on his hands. He was led by the arm into the living room, where the examination was conducted. When left alone he whined and chewed his hands, with the eyes tightly closed. He resisted relaxing his hands or the upper extremities. He appeared moderately well nourished.

The head was not deformed, and no cracked pot sound was elicited. Examination of the fundi was impossible, as he twisted, turned and whined while the eyelids were kept open by force. The pupils were dilated and responded well to light. There was no facial asymmetry. He appeared not to respond to loud sounds. The tongue and the cavity of the mouth could not be examined on account of his resistance. No paralysis of the extremities was detected. All tendon reflexes were present, and a definite Babinski sign was elicited on the left and a doubtful one on the right. The abdominal reflexes could not be obtained. The boy responded to pinpricks all over the body by rapid withdrawal and crying. In walking he carried his trunk and legs fairly normally.

He was reexamined on Dec. 8, 1935. The parents stated that the patient dressed and undressed and fed himself, was neat about his person and looked after his excretions without being reminded. He was somewhat restless at night and occasionally walked around the house. He played with his younger brother, who apparently dominated him. He was taking interest in the teaching that his older sister tried to carry out with him.

The patient shook the hand of the examiner. He appeared a trifle fearful but not in the least resistive. He took a chair opposite the examiner and submitted to an examination without resistance. He named the members of his family and enumerated the things he had eaten for breakfast correctly. He did not know the name of the street on which he lived; when informed of the name he was able partly to recall it fifteen minutes later. He had no recollection that he had been to school but knew his age. Occasionally, throughout the examination, he left the chair and joined his younger brother in play on the floor. He grabbed the toy locomotive from the brother and held on to it tightly. Articulation was clear, and attention was fair while it lasted. He was unable to solve any mathematical problem accurately. He named objects around him with relative ease, as well as pictures in a newspaper. He could not read or name the letters. He showed no emotional disturbance throughout the examination.

General nutrition was good, though he was thin. Examination of the throat, teeth, neck, chest and abdomen revealed no definite abnormalities. The cranial nerves were normal. Examination of the extremities revealed no disturbances in the motor, sensory, trophic, tonal, reflex or synergic spheres. The fundi were not altered. Gait and station were normal. The patient was not in the least awkward and could carry out complicated tests accurately.

Comment.—Because of a medicolegal situation, the patient was examined by several neuropsychiatrists; all agreed on one point—that they had never observed a similar case. Divergent opinions were expressed regarding the type of reaction and its etiology.

One examining physician stated that the child either was "defective" from birth or that he had had encephalitis and that the minor trauma was not an etiologic factor in the illness. Another expressed the belief that the type of reaction was caused by the minor trauma but that its intensity and duration were fostered by the household because of desire for compensation. He ascribed the improvement in the condition to the adjustment of the patient after a trial, and he

expressed the belief that final diagnosis should be deferred until the child had been observed and treated away from home surroundings. Other diagnoses were: juvenile dementia praecox, precipitated by trauma, and traumatic encephalopathy, with unusual manifestations.

We cannot give a definite diagnosis. The condition does not fit into any group in the authoritative classification of the psychopathologic sequelae of trauma proposed by Adolph Meyer (The Anatomical Facts and Clinical Varieties of Traumatic Insanities, *Proc. Am. Medico-Psychol. A.* **10**:106-177 [May] 1903).

DISCUSSION

DR. TEMPLE FAY: This case is of interest to me because I have to take a stand on a problem of the same kind. As I recall the history, the child received no injury of the head at the time; the accident was trivial, but the child was suddenly frightened. When I examined him, the boy showed the personification of a cat and meowed, scratched and clawed. He lay on a couch face down and kicked; there was no possibility of making an examination. He was like a little animal. I made a diagnosis of juvenile dementia praecox; that was when he was 9 years of age. He is now 11 and is far from recovery, although he has made a partial adjustment.

DR. GEORGE WILSON: When I saw this boy at the request of the insurance company, I frankly had not observed anything just like the condition. As Dr. Yaskin described the patient, he lay in a crouched position, with his hands over his face and mouth, and when I made an attempt to talk to him he sprang at me like a tiger and attempted to bite, claw and kick me. The father had a great deal of difficulty in restraining the boy. Psychoses in children are not common. This boy had a trivial head injury, if any. The family physician did not think there was much. The child apparently did not have juvenile dementia paralytica or acute mania. I could not elicit a Babinski sign, although it was difficult to examine the boy. I told the insurance company I did not know what was wrong with him and that it was only fair to hospitalize him. He was living in a typical city house, with a bed in the dining-room and no air or sunlight. His appearance now suggests that he may still live in the same quarters. The family was told that the company would take care of all expenses for treatment in a sanatorium, but consent to this was refused. I have the suspicion that perhaps the condition was built up by the father, although I have nothing on which to base it. The attention of the whole family centered about the boy. The offer to place him in a sanatorium was made before the trial. As I remember, the case was settled for $15,000, which if he has a traumatic psychosis is inadequate and if not, is too high. I am not convinced that the trouble is a traumatic psychosis. I do not think he has juvenile dementia praecox. The only real solution would be to put him in a hospital, away from his family, and observe him for a month or so. Without that, the whole matter is speculative. I do not think he suffered a severe injury of the brain, and I believe that the situation is more or less built up. He looks to me like a poor, undernourished, browbeaten child.

DR. FREDERIC LEAVITT: I read the testimony in this case; it reminds me very much of cases which Dr. Wilson and I observed in France, in part of a Negro section in action on the Argonne front. We had a number of patients in the field hospitals who presented just the picture of this boy. We called the disorder fright or shrapnel psychosis. The patients had been on front line duty for the first time, and trivial injuries paralyzed them with fright; they reacted just as in this boy's case. Instead of recovering when sent to rear line hospitals and home, they remained in the condition in which this boy is now.

DR. SAMUEL HADDEN: Have serologic studies been made? My reason for asking is that this patient resembles a child whom I saw in 1924; she presented the same type of behavior, characterized by biting, snarling and scratching; there was a history of an attempted assault by a neighbor boy. Prior to that time she had been normal; the symptoms had an acute onset. In the hospital serologic studies gave positive results. Every study of the mother and father gave and

still gives negative results. At the age of 3 weeks there had developed what was diagnosed as measles; however, it lasted two months. My colleagues and I think, therefore, that the patient may have had primary and secondary syphilis shortly after birth. The psychosis was of a definitely organic reaction type. This boy may have a condition of the same type.

DR. J. C. YASKIN: The Wassermann reaction of the blood was negative. My impression is that this is not a case of juvenile dementia paralytica. I am also convinced that the condition is a true psychosis. A brother of the patient died in the Philadelphia Hospital for Mental Diseases. It is probable that the injury precipitated a psychosis of organic character. I am convinced that the boy has a psychosis and also that the psychosis is organic. Regarding the most interesting part of the study, namely the management, I agree that he should be hospitalized and that more information should be secured to offset the possibility that the case is factitious. The parents refuse permission not only for hospitalization but for any kind of institutional care. However, the patient may have received better care at home, since he was definitely a nursing problem until a few months ago and might not have survived in an institution.

CASE OF HEPATOLENTICULAR DEGENERATION. DR. PAUL SLOANE.

S. C., aged 18, was studied at the Mount Sinai Hospital and later was admitted to the neurologic ward of the Temple University Hospital on Dec. 2, 1935, with the complaint of tremors of the head and upper limbs and disturbance of speech. The onset had been gradual. In February 1933 the patient noticed that her head shook while she was walking. This was followed shortly by tremors of both arms, which were exaggerated whenever she attempted to use the limbs. The tremors became progressively worse, so that on admission to the hospital she was unable to feed herself. Disturbance of speech was first noted in January 1935 and was progressive. At various times she complained of transient stiffness of the lower limbs, but there was no real impairment of walking. Incontinence of urine was present at times, particularly under the stress of violent emotion, but this was never a troublesome symptom. As the condition progressed the mother reported a definite change in the patient's personality. Whereas prior to the illness she was sweet-tempered and adjusted well with other members of the family, she then was moody and introspective and quarreled constantly with a sister. She became excitable; if not given immediately what she asked for she became violent and abusive and even threw things at persons. She became sensitive in respect to her condition and, because of awkwardness, refused to eat in the presence of any one but her mother. She was meticulous about her appearance and cleanliness and insisted on a change of clothes several times a day. She was always a good student but gave up school because of self-consciousness. She was fond of dancing and spent evenings in a neighborhood social center. Formerly, she had been popular with young people of both sexes, but after the condition became much worse she began to stay at home and grew more seclusive and irritable. She was discharged from the hospital in December and since has been observed in the outpatient department. At present she complains that the tremor has spread to include the jaw and that breathing has become jerky and irregular. At no time have there been remissions, diplopia or involuntary laughing and crying.

The patient was treated for acute catarrhal jaundice at the age of 9 years and made a complete recovery. The menses appeared first at the age of 15½ and were always irregular. She frequently missed a period for one or two months, and the flow was scant. A sister died of pulmonary tuberculosis at the age of 10 years; another died of Banti's disease at the age of 14 years. A brother, aged 27 years, died after an illness characterized by parkinsonian attitude and rigidity, intention tremors, jaundice and euphoria; no corneal pigmentation ring was observed; at autopsy hypertrophic cirrhosis of the liver and a large spleen, with perisplenitis, were observed.

Examination showed that the patient was fairly attractive and well developed. The secondary sex characteristics were well marked. There was some carious destruction of the teeth. The skin showed a peculiar pigmentation—diffuse darkness over the entire body, with many freckles of the addisonian type, in addition to peculiar depigmented spots and streaks, mostly on the back. No pigmentation was observed in the mouth. There was a supernumerary nipple on the left. The heart and lungs were normal. The blood pressure was 98 systolic and 70 diastolic. The liver was diminished in size, as determined both by palpation and by percussion. The spleen was not enlarged.

At rest no tremors were observed anywhere, but on walking a definite tremor of the head appeared. The Romberg sign was not elicited. Speech was jerky, scanning and tremulous. The patient had to exert considerable effort to enunciate clearly; as a result, speech was slow and labored. She had little control over the volume of her voice; at times it was loud and explosive and at others breathy and whispered. When the upper limbs were outstretched a coarse rhythmic tremor of the hands appeared, consisting of alternate flexion and extension at the wrists. The fingers were not involved. If the hands were supported by the examiner the tremor disappeared in the wrists and appeared in the arms and forearms, partaking of an oscillatory character of mild degree. As soon as the support was removed the tremor of the wrist returned. At times, however, the tremor disappeared of its own accord, even when the wrist was unsupported. In attempting to place the finger on the nose there was a violent, incoordinate throwing movement of the hand, and the patient instinctively guarded herself in order to keep from striking her face. The tremors were more marked in the left arm. There were also coarse flexion and extension movements of the left leg when the muscles were made taut. On talking or opening the mouth a coarse oscillatory tremor of the lower jaw appeared. All the tremors were exaggerated when the patient was emotionally disturbed. Adiadokokinesis was present bilaterally, and there was a fairly marked rebound phenomenon. There was no past pointing, however. Incoordination was characterized by marked clumsiness when the patient attempted to button her coat. There was no rigidity of any of the limbs; on the other hand, there was some hypotonia of the upper limbs, as evidenced by hyperextensibility of the elbows. The deep reflexes were universally diminished. The abdominal reflexes were present bilaterally, while the plantar responses were of flexor type. There were nystagmus on turning the eyes upward and nystagmoid movements on looking toward the right. At the sclerocorneal junction, almost entirely surounding the cornea, was a well marked ring of brownish pigmentation, which could be recognized even without the aid of the slit lamp. It was more marked at the superior and inferior margins, where it was about 1 mm. wide.

Mentally the patient was sensitive and showed great lability of affect. During the physical examination she appeared overly modest. In the presence of her mother she showed a great deal of impatience and irritability, particularly when the mother attempted to discuss her symptoms with the physician. At times she was sulky and had veritable outbursts of temper. She was moody and cried easily. She realized, she said, that her condition was becoming worse and expressed the belief that it was hopeless. She suspected that she was suffering from the same illness that her brother had and, as a result, became despondent at times. On one occasion, when she was presented before a class of medical students, she burst into tears, explaining later that she became discouraged with herself when she saw so many healthy young persons around her. She stated that she was fond of good times and was anxious to marry, although she added that she was aware that her illness would prevent her from marrying. She was eager to get away from home because her people teased her cruelly. Her sister, for instance, called her "diseased brain," while her father disapproved of her relationships with boys and referred to her as a prostitute. At times he even beat her for returning home late from a party. Her judgment was excellent, and there was no gross evidence of intellectual defect. There were no abnormal mental trends.

The blood count revealed: hemoglobin content 75 per cent, red cells 4,740,000, white cells 4,750 and differential count normal. Serologic tests of the blood (Kolmer, Kahn and Kline) gave negative results. The sugar content of the blood was 93 mg. per hundred cubic centimeters. The dextrose tolerance test gave a nearly flat curve, indicating greatly increased tolerance. The blood chemistry was normal (cholesterol 107 mg. per hundred cubic centimeters, serum calcium 10.9 mg. and inorganic phosphorus 5.6 mg.). The bromsulfalein test gave normal results, the five minute specimen showing 45 per cent retention, while there was no retention at thirty or sixty minutes. The galactose tolerance test gave normal results. The basal metabolic rate was —11 per cent.

The clinical picture in the case just described was characterized by violent, almost ataxic, intention tremors; scanning, explosive speech; a corneal pigmentation ring; absence of rigidity; emotional instability with marked irritability, and a small, hard liver. On the basis of these signs alone it is difficult to make a differential diagnosis between Wilson's disease and pseudosclerosis. Thus, although rigidity is considered part of the essential picture of progressive lenticular degeneration, some patients with Wilson's disease did not show this symptom until late in the course of the disease. For a time it was thought that the corneal pigmentation ring of Kayser and Fleischer appeared only in cases of pseudosclerosis, but Pollock reported it in a case of Wilson's disease in which the diagnosis was undoubted. The present case may therefore be an instance of the transitional forms which indicate the basic relationship between the two conditions and which led Hall to use the generic term hepatolenticular degeneration.

The resemblance to multiple sclerosis is evident in the occurrence of the intention tremors, nystagmus, scanning speech and cerebellar signs. On the other hand, however, abdominal reflexes are present, and there are no extra-ocular palsies, disturbances of sensibility, temporal pallor of the disks, peripheral scotoma or history of remissions. In addition, there are the history of a similar condition in a brother and the presence of a corneal pigmentation ring.

The history of preexisting jaundice has been described by others (Wilson, Luethy, Hamilton and Jones and Bostroem). The occurrence of Banti's disease in a sister may possibly be considered as a *forme frustée*, since this condition has also been described in association with hepatolenticular degeneration (Rystedt, Brückner and Schemmel). I have seen another case of pseudosclerosis, in which the diagnosis was verified by sections, in which splenectomy had been performed for relief of Banti's disease several years before. These facts have been utilized to support the theory that the cerebral symptoms are dependent on some previous damage of the liver, which permits a hypothetic toxin to circulate freely in the blood stream and thereby reach the brain. The toxin is supposed to have a special affinity for the cells of the lenticular nucleus.

The mental symptoms presented by the patient appear to be adequately explained by the emotional reaction to her disability. The social contacts have been restricted by her physical condition. At home she meets with scorn and ridicule, instead of sympathy and understanding. Her natural resentment finds outlet in a desire to escape, the opportunity for which is offered by marriage. She realizes, however, that her condition will prevent her from marrying, and her moral standards will not permit her to gratify an apparently strong sex drive. In addition she senses that her illness is similar to that which caused the death of her brother and that it is becoming progressively worse. What, then, is more natural than for discontent to be manifested in the form of irritability and overemotionalism? At no time has there been any evidence of dementia or inexplicable emotional reactions; it is unnecessary, therefore, to implicate any structural changes in the brain to account for the mental picture.

The menstrual irregularity is evidence of a profound endocrinal disturbance and has been mentioned by others. In addition, there are the peculiar pigmentation of the skin, greatly increased sugar tolerance, low blood pressure and slightly

lowered basal metabolic rate. These signs recall the picture of Addison's disease, which might be considered but for the absence of general weakness and debility, anemia, feebleness of heart action and gastro-intestinal disturbances.

DR. J. YASKIN: What were the pyramidal tract findings?

DR. P. SLOANE: There was apparently no involvement of the pyramidal tracts. The deep and superficial reflexes were normally active and equal, and there was no Babinski sign. Although the patient has scanning speech, nystagmus and intention tremors, there have been no remissions since the onset three years ago. In addition, the presence of the corneal pigmentation ring is sufficient to rule out multiple sclerosis.

"JAW WINKING." DR. TEMPLE FAY and DR. MICHAEL SCOTT.

A woman, aged 52, single, had first been admitted to the Temple University Hospital on Oct. 10, 1934, to the service of Dr. Matthew Ersner, with the complaint of right suppurative otitis media and mastoiditis. There was a history of an operation on the mastoid seven years before her first admission to the hospital, and the patient had noticed deafness in the right ear for at least twenty-five years. On Oct. 18, 1934, a radical mastoidectomy, with excision of a post-auricular fistula and removal of a cholesteatomatous mass, which involved the entire mastoid cavity and middle ear, was performed by Dr. Ersner. Seven days later complete reaction of degeneration was found in the distribution of the right seventh nerve. On Dec. 4, 1934, a Ballance-Duel operation was performed by Dr. Ersner; a portion of the anterior femoral cutaneous nerve was sutured to the peripheral and central ends of the right facial nerve. Twelve days later blepharorrhaphy was carried out by Dr. Walter I. Lillie.

The patient was readmitted to the hospital to the neurosurgical service of one of us (T. F.) on Jan. 21, 1936 (thirteen months after the Ballance-Duel operation), because of dizziness and attacks of falling. She presented typical peripheral paralysis of the right facial nerve. There was evidence of right blepharorrhaphy. The pupils were equal and regular and reacted to light and in accommodation. The extra-ocular muscles and visual fields showed no abnormality. The other cranial nerves were essentially normal. The deep tendon reflexes were bilaterally equal and active. The Babinski and Hoffmann signs were absent. Sensation, coordination and muscle power were not impaired.

Laboratory studies, including urinalysis, blood counts and estimation of blood sugar, gave essentially negative results. The Wassermann and Kahn reactions of the blood were negative; the reaction to the Kline test was + 1. Studies of the spinal fluid gave normal results.

Roentgenography of the right mastoid region showed evidence of the previous operative procedure but nothing suggesting acute pathologic change. Dr. F. L. Follweiler reported that the patient had little or no hearing in either ear and that he was unable to secure cooperation for an audiometer test.

On Bárány examination Dr. J. Winston found that there was occasional spontaneous rotatory nystagmus to the left on looking down. Neither the cochlear nor the vestibular portion of the right eighth nerve appeared to function. The vestibular mechanism on the left responded promptly, although hearing was markedly impaired in this ear. Dr. Winston expressed the belief that these findings suggested a peripheral lesion of the right eighth nerve.

The following observations were made by one of us (T. F.) on March 14, 1936: "This morning the patient had a great deal of function on the right side of the face. When the command to close the eye was given, not only did the right corner of the mouth draw up but, even with the wink reflex on the left, there was a definite coordinated jerk or twitching at the lower angle of the mouth on the right. When the patient forcefully closed the eye, the effort gave a response in the lower two thirds of the face, and on two occasions the entire right side of the face was brought up almost to a normal degree, although the duration of this movement was extremely brief—power being greatly diminished. When instructed to draw up the corner of the mouth, the patient showed a slight twitch-

ing movement beneath the right eye, and it was obvious that the condition was that known as 'jaw winking' and that regeneration had occurred in the field The most interesting fact was that the spontaneous wink reflex on the left was manifested to the lower angle of the mouth on the right."

Dr. Ernest Spiegel, in endeavoring to correlate the response of muscles innervated by the seventh nerve to segmental stimulation of the trigeminal nerve found that twitchings of the muscles about the mouth on the right side can be elicited not only by touching the conjunctiva of the left eye but by faradic stimulation of the skin in the area of the first branch of the fifth nerve on the left. On faradic stimulation of the second and third branches of this nerve, no contraction of the muscles about the right half of the mouth was observed. It is possible that such a contraction escaped the observer, owing to the fact that the powerful contraction of the muscles on the left side of the face pulled the mouth and the neighboring skin to the left.

The reaction of degeneration was studied by Dr. F. L. Follweiler on March 26, 1936: There was a definite reaction to faradism, which was, however, diminished. There was a response to faradism of approximately from 10 to 15 per cent. Response to galvanism was considerably more acute than when tested on Oct. 26, 1934. This patient showed distinct improvement in nervous and muscular response.

DISCUSSION

Dr. Temple Fay: The thing of interest in this case was that the fibers which apparently supply the right eyelid for the wink reflex caused involuntary jerking in a small group of muscles about the corner of the mouth. There seems to be selectivity. I have seen the voluntary closure of the eyes produce pulling up the face on the recently paralyzed side, but involuntary winking of the eye associated with pulling up the lower corner of the mouth on the right seems to indicate that there is a selectivity in regrowth of the fibers.

Dr. Ross Thompson: I recently found that an author has expressed the belief that nerves regenerate about 1/28 inch (9 mm.) in twenty-four hours. Operation was performed sixteen months ago on this patient; hence, it seems that regeneration should be established by this time throughout the course of the nerve.

Dr. Abraham Ornsteen: Is there any improvement in the cosmetic appearance, and is the drooping less marked?

Dr. Michael Scott: Dr. Ersner can answer the question as to improvement in the cosmetic appearance. It has been so short a time since massage and treatment with the sinusoidal current were started that we cannot say that there has been any definite improvement.

Dr. Ernest Spiegel: The fibers that regenerated first in this case are those which are functionally most important, for they protect the eye. It seems that these fibers regenerate in two directions, partly toward the eye and partly in an abnormal direction, toward the mouth. The difference between the voluntary and the reflex reaction is only quantitative. Boeke's experiments shed light on the question whether sensory nerves may be used for regeneration of motor nerves. He showed that there is practically no difference between motor and sensory nerves for purposes of regeneration. Sensory fibers may be connected with motor nerves and vice versa.

Dr. Matthew Ersner: Repair of an injured facial nerve is at times discouraging; it takes place so slowly that waiting for improvement becomes irksome. The operation performed on this patient followed closely the work of the late Dr. Arthur Duel and Sir Charles Ballance. The procedure is as follows: A sensory nerve, usually the anterior femoral cutaneous, is isolated and cut and then allowed to remain in situ, while it undergoes wallerian degeneration. This requires about three weeks. The point of incision of the nerve is marked with black silk thread, and a piece of thin gold-foil is wrapped about the cut ends.

When the patient is ready for the nerve graft, the descending portion of the facial nerve is exposed completely. The injured point is located. In this case

we observed that it was injured just below the horizontal semicircular canal, beneath the mastoid antrum. This is a frequent site of injury in cases of radical mastoidectomy. The injury dated back seven years and followed the performance of a radical mastoidectomy in another city. We observed the nerve to be a mass of scar tissue at this point. The tissue was removed, and the nerves were cut and the ends freshened. The anterior femoral cutaneous nerve was then located, and about 6.8 mm. of the nerve was anastomosed end to end. The graft was then covered with a small piece of gold-foil. Slight improvement has been noted up to the present, as has been demonstrated.

The important point to bear in mind is that it is not necessary to utilize motor nerves in order to repair an injured motor nerve.

CONTROL OF MICTURITION BY THE CENTRAL NERVOUS SYSTEM. DR. ORTHELLO R. LANGWORTHY, Baltimore.

After injury of certain groups of cells or fibers in the central nervous system there are characteristic changes in the tone and contraction of the smooth muscle of the bladder, which can be recognized in graphic records. Evidence was obtained both from experiments on animals and from the study of patients. The tone and contraction of the smooth muscle of the bladder are dependent on the activity of the stretch response. The stretch reflex in the vesical muscle is hyperactive after injury of the corticospinal tracts and is lost after injury of the posterior sacral roots.

To make the graphic records a catheter is placed in the bladder and connected by means of a T-tube with a source of fluid and an air-water manometer. The manometer records on a kymograph by means of a tambour. The fluid is usually added to the system in unit quantities. This is an adequate stimulus for the stretch response.

With injury of the posterior sacral roots, such as that in tabes dorsalis, the bladder holds large quantities of fluid at low intravesical pressures. The contractions of the muscle are impaired. Small, rhythmic waves of vesical contraction, showing little tendency to summation, appear in the records when the anterior sacral roots which carry the parasympathetic fibers are destroyed. These waves are often observed in records made from patients with vesical symptoms dependent on spina bifida.

Patients with involvement of the corticospinal fibers complain of urgency and frequency of micturition. The frequency is due to the small vesical capacity; urgency is associated with hyperactivity of the stretch response. The resting intravesical pressure is high. As filling nears completion afferent stimuli from the bladder may initiate rhythmic contractions of the cremasteric muscles and of the paralyzed legs.

Injury of the lateral columns of the spinal cord involving both the corticospinal fibers and the pathways from the brain stem controlling tone in the vesical muscle produces more severe abnormalities of micturition. Rhythmic contractions of large amplitude occur throughout filling. These waves are poorly sustained and are inefficient in emptying the bladder.

Damage to the cerebellum causes hesitancy of micturition and periods of acute retention. The vesical capacity is increased, and the contraction at the end of filling is weak. Similar changes in bladder function have been observed in animals after removal of portions of the cerebellum.

Some patients with the parkinsonian syndrome complain of frequency of micturition. The resting intravesical pressure is high, both in the empty bladder and during filling. The vesical capacity is small. There is no hyperactivity of the stretch reflex.

DISCUSSION

DR. MAURICE MUSCHAT: This presentation is precise and opposed to the archaic discussions of the "neurogenic bladder" by the urologist and the neurologist. Certain definite data have been obtained, which unquestionably will lead much

further. This work is a boon to the urologist, for years ago when the medical or neurologic service asked the urologist to diagnose a neurogenic condition of the bladder he could do so only by exclusion. If he did not find obstruction or evidence of stone he presumed that the condition must be due to disturbance in innervation. Today he is able to say more to the referring physician. He can give a graphic presentation of the stretch reflex or of the actual status of the detrusor muscle of the bladder. The question is how far one has gone in giving more than the mere diagnosis of a neurogenic condition of the bladder. A stage is reached at which more is demanded, and more can be given. My associates and I use a mercury cystometer; we do not use a water manometer, as it is more complicated and is too cumbersome at the bedside. We obtain three factors by cystometric examination: (1) the pressure at which there is desire to void, (2) the actual character of the curve and (3) the maximal voluntary pressure.

The desire to void occurs normally at pressures between 150 and 275 mm.; when it occurs at less than 150 or more than 275 mm., the condition is neurogenic. The curve is one that ascends gradually; when it is very high or very low the condition is neurogenic. The maximal voluntary pressure is between 40 and 70 mm.; when it is under 40 or over 70 mm. the condition is neurogenic.

Cooperation is essential; for instance, a young woman, recently married, complained of severe frequency of urination; examination of the urine did not show pus, and cystometric examination revealed a neurogenic condition of the bladder of hypertonic type. She was referred to Dr. B. J. Alpers, who made a diagnosis of multiple sclerosis. By carefully following this work the urologist is able to aid the neurologist in the quest of a proper diagnosis in neurologic disorders.

Dr. Ernest Spiegel: I can point to experiments made some time ago. Dr. Lichtenstein claimed that a subcortcial center of the bladder is located in the region of the corpus subthalamicum; according to Karplus and Kreidl the corticifugal fibers to vegetative organs are interrupted in the region of the corpus subthalamicum. After interrupting the extrapyramidal systems, Dr. W. Hunsicker Jr. and I found that cortical impulses still reach the bladder; we concluded that there must be a pyramidal as well as an extrapyramidal conduction of these impulses. Dr. Langworthy's findings that in cases of lesions of the corticospinal tract and extrapyramidal centers disturbances of the bladder are detected seem to be in excellent agreement with these experimental results. I was particularly interested in the parts of Dr. Langworthy's paper which dealt with the effect of reflexes from the bladder on skeletal muscles. We made similar experiments, stimulating the splanchnic nerve in decerebrate cats, and found that it definitely increased the tone in muscles of the extremities. Similar work was done by Langelaan on frogs. When one speaks of centripetal impulses one deals not only with reflex phenomena but with conscious sensations, in human subjects at least. How does the impulse from the bladder reach the cortex? Dr. Hunsicker and I, in a study of these questions, stimulated the centripetal nerves of the bladder by dilating the bladder, which was enclosed in a capsule so that no other organ was stimulated. We showed that in the cat such stimulation produces definite changes of potential in the thalamus and the cerebral cortex. It seems therefore, that in the cat afferent impulses from the bladder also reach the cerebral cortex by way of the thalamic system.

Dr. Langworthy: Urologists would obtain more information by use of the air-water manometer, as it gives more delicate responses. The air-mercury manometer, of course, presents fewer technical problems.

Dr. Spiegel discussed the problem of afferent pathways in the central nervous system controlling micturition. A study of these pathways has not been completed. In the first case of the thalamic syndrome described by Dejerine, symptoms of extreme urgency of micturition were shown for the first few weeks after the vascular accident. Holmes and Sargent described cases of thrombosis of the superior longitudinal sinus in which disorders of micturition were dependent on impairment of normal vesical sensation.

In reply to the question of Dr. Alpers: I think that the changes in vesical function after injury of the cerebellum or its pathways are dependent on loss of tone in the smooth muscle of the bladder.

SITE OF ACTION OF ACETYLCHOLINE AND ITS SIGNIFICANCE. DR. H. G. WOLFF, New York.

Since acetylcholine is closely identified with the cholinergic agent elaborated during autonomic nerve function, its properties assume particular importance, and its site of action has especial significance. It has been commonly assumed, though never completely demonstrated, that acetylcholine acts directly on the peripheral tissues innervated by parasympathetic nerves. The current assumption concerning the direct action of acetylcholine has recently been questioned by Armstrong, who made the observation that when the embryo Fundulus heart is aneural its threshold for acetylcholine is higher than physiologic limits. Moreover, when functional innervation of the heart does occur the heart responds to minute amounts of acetylcholine. From this it was concluded that acetylcholine exerts its effect on the parasympathetic ganglia or the postganglionic nerves and not on the cardiac muscle itself.

Unfortunately, in the adult heart it is impossible to remove the outlying parasympathetic ganglia, so that the Armstrong experiment cannot be repeated with adult tissue. The mammalian eye, however, is suitable for investigation of this question, since the parasympathetic (ciliary) ganglion can readily be removed. Engelhart showed that the iris in the cat contains a cholinergic substance resembling acetylcholine and that stimulation of the oculomotor increases the cholinergic substance within the iris. Constriction of the pupils simultaneously with an increase in cholinergic substance suggests that the two changes are related.

Hence, in an attempt to demonstrate the actual site of action of acetylcholine in the eye, the following experiments on cats were carried out: The ciliary ganglion was removed and subsequently identified by histologic examination. In 4 animals, immediately after removal of the ciliary ganglion, a slit was made in the margin of the cornea, and some of the fluid of the anterior chamber was allowed to escape. This usually caused the dilated pupil to become slightly narrower. When equilibrium had been reached, a needle was inserted in the anterior chamber and 0.1 cc. of a 1:1,000,000 solution (0.1 microgram) of acetylcholine bromide was injected. Constriction of the pupil occurred within from fifteen to thirty seconds and was complete within a minute. As a control 0.1 cc. of Ringer solution was injected several times. The Ringer solution and needle produced slight or no effect on the size of the pupil. These experiments demonstrate that acetylcholine is effective in the eye when directly applied to the iris in the absence of the ciliary ganglion.

To ascertain whether the constriction of the pupil was due to the action of acetylcholine on the radial muscle or the parasympathetic nerve endings, the postganglionic parasympathetic nerve fibers were allowed to degenerate after removal of the ciliary ganglion in 3 additional cats. The pupil of the side on which no operation was performed served as a control. After from six to twelve days the dilated pupil on the deganglionated side showed no constriction after conjunctival instillations of a 1 per cent solution of physostigmine salicylate; the previously described procedure of slitting the cornea, controlling with Ringer solution and injecting 0.1 microgram of acetylcholine bromide in solution into the anterior chamber of the eye was repeated. Constriction of the pupil was again prompt and complete, except where it was partially impeded by adhesions of connective tissue. After atropinization, acetylcholine no longer had any effect. In one cat the eye was removed and the iris studied in vitro. Though of a similar nature, the results were less satisfactory than those of the experiments in vivo.

These experiments demonstrate that, at least for the iris of the cat, the action of acetylcholine is peripheral to the postganglionic fibers and presumably direct on the radial muscles. This is of interest in relation to the experiments of Armstrong indicating that embryonic muscle does not acquire its sensitiveness to acetylcholine until after cholinergic nerves have reached it. In generalizing from both types of experiments, it appears that the physiologic properties of the muscle (adrenergic or cholinergic) are bestowed by the proximity of specific nerve fibers and that, once acquired, the specific sensitiveness is retained, at least for a time,

after degeneration of the nerve fibers. Since it is probable that many smooth muscle fibers do not receive direct nerve connections, it is necessary to assume that the nerve has a sphere of influence in functional differentiation which extends beyond its terminations. This influence may be analogous to the effect of neighboring cells on structural differentiation, of which there are many examples in experimental embryology.

These preliminary observations permit of no conclusion as to whether the response to acetylcholine is retained permanently in the absence of the parasympathetic nerve supply.

DR. E. SPIEGEL: Dr. Wolff worked successfully on an interesting problem. Since the work of Loewi on the nerves of the heart, one has reached a new conception in regard to the action of peripheral nerves on the end-organs. Dr. Wolff stated that acetylcholine has been found to be a powerful substance. It acts on the heart, producing an effect similar to that of the vagus nerve, namely inhibition. Since these nerve actions take place through the medium of a chemical substance in the periphery, one can perhaps understand the mechanism of the antagonistic behavior of nerves, which may be produced by the action of different chemical substances. The question arises whether inhibition in general may be explained in a similar way. There exists a central type of inhibition, apparently due to interference of two or more sets of impulses. Reflex inhibitions belong to this group. Since more is known about the action of the peripheral nerves, the question arises whether this central form of inhibition may also be due to chemical action. May I ask Dr. Wolff whether he has some special experience concerning this point?

DR. H. G. WOLFF: A question concerning prostigmin (dimethylcarbamic ester of 3-oxyphenyltrimethylammonium methylsulfate) and its action in myasthenia gravis was raised. It would be premature to offer any explanation of this action, but I can at least present for consideration such data as there are. Prostigmin is similar to physostigmine. This accentuates and prolongs the action of acetylcholine. It has been shown that stimulation of the preganglionic and postganglionic parasympathetic fibers and some of the postganglionic sympathetic fibers results in the production of acetylcholine. Acetylcholine is also produced when a somatic motor nerve is stimulated (Dale). It is not known with certainty whether this agent is what causes the contraction. However, with this in mind, physostigmine was tried, in an attempt to discover whether it would improve muscle function in cases of myasthenia gravis. It does. How it acts is uncertain. Acetylcholine in physiologic doses, when injected into the lateral ventricles, causes a change in respiration similar to that produced by central stimulation of the vagus nerve (Dikshit). From this one may postulate that acetylcholine may have its action not only on the sites mentioned but on central structures as well.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, April 16, 1936

STANLEY COBB, M.D., *President, in the Chair*

CONSIDERATION OF PERSONALITY AND SOCIOLOGIC FACTORS IN THE CARE AND TREATMENT OF PERSONS WITH CHRONIC ALCOHOLISM. DR. KENNETH J. TILLOTTSON.

This article will be published elsewhere.

TWO PATIENTS WITH POSTENCEPHALITIC PARKINSONISM ASSOCIATED WITH PSYCHOSES. DR. JOHN B. MCKENNA.

Soon after the World War and the epidemic of influenza in 1918, numerous cases of postencephalitic parkinsonism began to appear. These afforded con-

siderable opportunity for neuropsychiatric study from many angles, including not only the mental complications in the acute phases of encephalitis but the more important condition of mental abnormality accompanying the postencephalitic states.

It has been common experience that euphoria is a frequent symptom of postencephalitic parkinsonism. Almost invariably the feeling of mental well-being of the patient is disproportionate to the seriousness of the physical symptoms. In by far the greater number of cases, however, there is no outspoken psychosis; the presence of this complication is always noteworthy, despite the fact that reports of a considerable number of cases in which it occurred have already appeared in the literature, especially since 1921. These contributions have dealt largely with the fact that many types of psychotic reactions have been observed, and many facts which might aid in the explanation of the actual relationship between the organic disease process and the psychotic manifestations have been presented.

Hohman (Epidemic Encephalitis [Lethargic Encephalitis]: Its Psychotic Manifestations with a Report of Twenty-Three Cases, ARCH. NEUROL. & PSYCHIAT. **6**:295 [Sept.] 1921) made a detailed report, in which he called attention to nine postencephalitic mental syndromes. He grouped these into four reaction types: depressive, delirious and organic and those resembling a psychoneurosis. He concluded that there were no definitely formulated and persistent trends but that the prepsychotic personality of the patient largely determined the type of the psychosis. Rhein and Ebaugh (*Am. J. Psychiat.* **3**:791, 1924) subscribed to this opinion, after Kirby and Davis, Jones, Steck and, later, Alpers had given numerous illustrations of Hohman's contention. Strecker and Ebaugh (Practical Clinical Psychiatry for Students and Practitioners, ed. 4, Philadelphia, P. Blakiston's Son & Co., 1935) referred to 30 cases in which this fact was likewise apparent. Hohman stated that with a diffuse organic change, such as that produced by encephalitis, the personality or constitution of a person is likely to rupture at the point of greatest vulnerability. On the contrary, Cholpicki, in Germany, pointed out in 1931 that in only 1 of his 6 cases of extreme anxiety states associated with postencephalitic parkinsonism was there evidence of unusual anxiety in the previous mental life of the patient.

Bromberg in 1924 reported 135 cases of abnormal mental states in association with chronic encephalitis and called attention to the close similarity with pictures of recognized psychiatric entities. In a large group of his cases the behavior was characterized by antisocial conduct, but personality changes were more common in children. Depressions were most common in affective reactive types. In the cases of schizophrenia the accessory rather than the fundamental symptoms of schizophrenia were present. He found also that in cases in which paranoid-hallucinatory states existed the psychosis was usually transient.

Rhein and Ebaugh laid emphasis on the affective disorder in postencephalitic states in children and found suicidal attempts frequent, though usually lacking definite motivation. Such depressive trends were transient and showed an absence of the type of depression observed in manic-depressive psychoses.

Bond and Partridge (*Am. J. Psychiat.* **6**:25, 1926) first called attention to the important aspect of the management of postencephalitic behavior in boys. In an intensive study of a large group of boys with this disorder, they found that there was a direct relation between the severity of the physical injuries and the behavior difficulties. They found that the boys were manageable as a whole and that their behavior improved greatly in response to simple methods of discipline. A similar type of work is still being carried on by Strecker and Ebaugh, with satisfactory results.

An almost uniform finding in the literature dealing with postencephalitic behavior difficulties in children is the intellectual enfeeblement or arrest if the original attack of acute encephalitis occurred at the age of 3 years or earlier.

In the past five years numerous additional articles dealing with postencephalitic psychoses have been, for the most part, confirmatory of the points already brought

out. In practically every instance reported the development of the mental disturbance occurred pari passu with that of the physical symptoms, so that the relationship between the two can hardly be questioned. The nature of this relationship, however, is by no means settled.

It is hoped that the 2 cases to be described will add a link to the chain of evidence which may eventually lead to an explanation of the psychopathologic nature of the psychomotor manifestations. In these 2 patients, who were treated by my associates and me in recent months, different mental states were demonstrated; in 1 instance the relation between the psychotic manifestations and the prepsychotic personality was clearly illustrated. Furthermore, this case seems to support the contention that a "personality or constitution able to maintain an adequate adjustment with the proper repression or sublimation of unsocial trends or of strong instinctive drives breaks along these lines when the automaticity of adjustment is interfered with". (Hohman).

CASE 1.—A boy aged 15, of Irish and Italian parentage, was transferred to the McLean Hospital from the Boston Psychopathic Hospital on Jan. 2, 1936. At the latter hospital he had become noisy and aggressive and apparently had been hallucinated. The present illness began in March 1935, when, one month after the surgical drainage of a rectoperineal abscess, he became more restless than usual, shifted his interests rapidly and became careless about his person. During the following summer these altered habits became more marked.

In September 1935 he matriculated at the Lawrence Academy, where during the first few days he had to be reprimanded for loud talking. He gradually became more tense. The headmaster reported that early in October the boy suddenly insisted on going home to see several girls, with whom he was in love. When the request was refused, he became resistive, yelling and disturbing the school. He later complained to his parents and local physician that people were trying to hypnotize him. At home he was eager for bed; for four days he wanted to sleep most of the time and complained of headache. His temperature was 99.2 F. At the Peter Bent Brigham Hospital, where he was taken for study, skull plates, an encephalogram and lumbar puncture revealed no abnormality. Because of continued restlessness care at a hospital for mental diseases was suggested, but the parents took him home, where to them he seemed normal again. However, on October 30, he suddenly became noisy, irritable and demanding. The next day he ordered people from his room on the slightest provocation, was irritated by ordinary sounds and accused his mother of hypnotizing him. He was taken to the Boston Psychopathic Hospital, where he continued to be resistive and uncooperative and incontinent of urine and feces. He refused food. He was irrelevant, querulous and apprehensive, complaining of machines which caused him to see pictures on the wall. These ideas of influence soon receded. He slept and ate excessively at times. He was often rude, seclusive and undertalkative, but later he became active and inquisitive. He was precocious mentally, preferring to calculate with a slide-rule rather than take part in games. Psychometric examination with the Stanford test showed a mental age of 17 years and 3 months. Motor coordination was observed to be poor. Laboratory examinations gave normal results. The diagnosis of dementia praecox was made.

On transfer of the patient to the McLean Hospital, an anamnesis furnished by his mother revealed the following important points: The family history was irrelevant. The patient was the eldest of 3 children, the other 2 of whom seemed normal in every respect. He was born a "blue baby" and at the age of 6 weeks suffered an attack of what was suspected to be meningitis. He spoke a few words at the age of 10 months and walked well when 15 months old. At the age of 3 years he suffered an illness which was described as follows: One morning he preferred to remain in bed, which was unusual. There was definite elevation of temperature, although the exact degree was not remembered. A local physician could find no explanation for the condition. During the next three days

he slept constantly but was easily awakened, although he often dozed while taking food or in the midst of answering a question. On the fourth day he was considered normal.

From that time he seemed peculiar in that he never cared to play outdoors but preferred to read, usually *Popular Mechanics* and similar scientific magazines. On entrance to school he was seclusive and showed no interest in games, although he indulged occasionally in individual athletics, such as skiing and coasting. He always liked microscopes and telescopes, and since the age of 5 years he has used a typewriter for practically all writing.

At school he did excellently until he reached junior high school, when his lower grades were attributed to inability to write without a typewriter. He was slow in writing examinations. His mother observed that "his fingers did not coordinate with his mind."

A brief review of his usual personality brought out the fact that from earliest childhood he was neat, quiet, obedient, affectionate and generous. He had no close friends and was restless without his books. There were no changes in mood. He always learned easily, had a good memory, used excellent English and had a keen sense of humor. His enthusiasm for anything scientific and his seclusiveness have already been mentioned.

In addition to the illnesses in early childhood which have been mentioned, he suffered the usual diseases of childhood, without complications; he underwent appendectomy at the age of 8 years and had a fracture of the ankle at 13 and the rectoperineal abscess already mentioned.

Examination on admission to the McLean Hospital showed a tall, thin, rangy boy, exhibiting aimless, restless curiosity. He was facetious, aggressive, impolite and rude. His stream of talk showed patchy spontaneity, with periods of muteness, a tendency to wander and some motor hyperactivity during speech but no definite retardation or flight of ideas. He was irritable and boastful but not particularly depressed or elated. He was preoccupied with many shifting interests and dismissed specific inquiries with short sentences, interrupted by great motor activity, as he moved about the room and frequently requested the examiner to "scram." Orientation and memory were good, and the sensorium was intact. He had no insight or judgment. General physical examination gave normal results. Neurologic examination showed: failure of convergence of the eyes, occasional tremor of the neck, absence of the blinking reflex and a slow rhythmic tremor of the left arm, with rigidity of the flexor and extensor muscles. The cogwheel phenomenon was present. He used his left hand rather than his fingers in pointing and showed slight clumsiness in the use of the left arm, with decreased associated movement. There was also diminished strength in the left leg, with a weakened knee jerk.

Since his admission to the hospital the patient has continued to show eccentric behavior. For the first few weeks he was restless, rude to every one and continually on the go. The difficulty in using the left hand became more apparent, and the other neurologic signs persisted. However, he obeyed instructions well. It became obvious that whenever he was unoccupied he was erratic. He was a distinct trouble-maker in the ward, often attempting to fight with the nurses and patients. This necessitated removal to a ward for disturbed patients, where he immediately complained of vague aches and pains, without demonstrable cause. Soon, with the institution of a daily routine of various activities, his behavior showed slight but definite improvement. He made little objection to mild discipline or reprimands about his behavior and spontaneously promised to try to do better. This improvement, however, was frequently interrupted by short periods of restlessness, excitability and rudeness. Although he is at present definitely abnormal, he shows a distinctly better behavior than at the time of admission. He utilizes his free moments in working his slide-rule and studying algebra and chemistry.

There is little room for doubt of the diagnosis in this instance. Among other things, the case brings out the necessity of studying the patient not only from one point of view but from the standpoint of the total symptomatology, through the psychobiologic approach. It would be interesting to know how long this boy's

neurologic symptoms have existed and whether they have anything to do with the original attack of encephalitis at the age of 3 years or are related to a new attack last year. These symptoms probably would not have been evident to his parents, although the awkwardness in using the left arm and hand was observed several years ago. The onset of psychotic symptoms had an acute onset twelve years after the original attack, but there was evidence of a distinctly peculiar personality from early childhood. Even in the absence of an acute process in the summer of 1935, one sees many other factors in force at the same time—the operation, a new adjustment at school and the onset of puberty—stresses which can be easily mishandled by an already damaged nervous system. Although there was certainly no intellectual enfeeblement or arrest in this instance, the peculiar personality confirms the findings in most other cases observed in children.

CASE 2.—A man aged 52, an American, married, a pharmacist and chemist, was admitted to the McLean Hospital on Jan. 30, 1936, with the complaint that he had been depressed for two months, with gradually increasing apprehensions. The present illness had a vague onset about five years before, when in the face of uncertainty about his future he became restless and nervous and worried over the accuracy of his work. Through no fault of his own he had to seek new employment and was engaged to do food analysis. He continued to worry over accuracy in this work and its effect on others. After a week he left the position and became suspicious of the high recommendations given him. His apprehensions increased, and he became morbidly oversolicitous about the health of his son and wife. After a short period of spontaneous improvement, he began to show poor concentration and obsessions about the furnace fire, locked windows and the like. A few days before he had thrown mercury bichloride into a cesspool; soon he became convinced that it had made its way into the water-main and had poisoned the whole town, including his son. He became intensely agitated about this and insisted on confessing his crime to the board of health. He became sleepless. He said that people were after him to poison his food, burn his house and attack him. He agreed that he should go to a hospital and expressed a vague realization that he was mentally ill. He willingly accompanied his wife to the hospital.

The family history was irrelevant except that the father, also a druggist, was a chronic addict to the use of alcohol and divorced his wife when the patient was 26 years of age.

Birth and early development were normal. After graduation with highest honors from the Massachusetts College of Pharmacy at the age of 22, the patient began work in his father's drug store. At the age of 29 he was engaged as assistant chemist and later as chief chemist by a large food manufacturing company. He was respected by both supervisors and subordinates. He married at the age of 28, and his married life was described as unusually congenial and satisfactory, both socially and sexually. He had one son, aged 18 years, who appeared to be normal.

In 1919 he suffered a rather severe attack of influenza, without complications. In 1923 he suddenly became acutely ill; he had double vision and general malaise but no other specific symptoms. He remained in bed for one month, during which he slept fifteen hours every day, though he was easily aroused, only to doze off again after a few seconds. He was well after three months. On close questioning the patient's wife recalled that since January 1935 he had not walked as erect as usual, that he occasionally stumbled in going upstairs and that during the few weeks prior to his admission to the hospital it was increasingly difficult to get him to smile.

A discussion of his prepsychotic personality brought out that he was of an unusually sunny disposition and a good mixer but had always been overmodest about his abilities. He had never had definite swings of mood. He was always apprehensive, overconscientious and fussy. In his work as a pharmacist and chemist he had always felt it necessary to check and recheck his results and to institute many ritualistic procedures in order to insure against possible errors. He was oversensitive about the opinions of others.

On admission to the hospital examination revealed a thin, wiry man of medium size, who was acutely apprehensive. The skin was moist, and the extremities showed mild tremor. The facial expression was rigid and fearful. He walked with loss of associated arm movements, flexed elbows and short, careful steps. His head was slightly flexed on the trunk, and the whole body moved stiffly as he looked from side to side. He showed the phenomena of propulsion and retropulsion. The execution of any movement was performed with deliberate slowness. The pupils were slightly irregular and reacted sluggishly. There were almost complete loss of the blinking reflex and absence of convergence of the eyes. There were a distinctly "doughy feeling" in the arms and definite cogwheel rigidity. There was evidence of involvement of the pyramidal tracts.

Except for a loud systolic murmur over the mitral area, faintly transmitted to the axilla, and blood pressure of 165 systolic and 80 diastolic, general physical examination gave essentially normal results. Laboratory examinations revealed nothing abnormal.

The mental status was as follows: The patient was bewildered and apprehensive, with some willingness to cooperate. There was a slight pressure of speech, with an emotional reaction, chiefly of fright. There was no definite depression. The mental trend dealt with a review of his work and the fears of persecution because of the imagined results of his errors, which have already been mentioned. He revealed no hallucinations and was well oriented in all spheres; the sensorium was intact. He had no insight into his condition.

For the first few days he continued to be apprehensive and restless and required constant watching. His anxieties became more marked, and he repeatedly requested that he be allowed to leave the hospital in order to reassure himself that people were not being poisoned by water. On the fifth day he was fearful that bizarre sexual assaults on him were being planned, and that evening he made a suicidal attempt, with the result that he was transferred to another ward.

At this point therapy with scopolamine hydrobromide was begun. He continued to be apprehensive, restless, sleepless and suspicious and complained of hearing voices. He believed that other patients talked about him, that he was being poisoned and that he had made sexual assaults on other men. He heard the cries of his wife and son, who were being tortured in the basement. Slowly he began to improve. The mental symptoms diminished concomitantly with the decrease of all parkinsonian symptoms. The hallucinations ceased, and he became cheerful, more spontaneous and less apprehensive, although occasionally he inquired rather sheepishly about his wife's health. He was occasionally restless at night, with mild apprehensions about her, but with insight. He was able to joke about his symptoms. It is of interest that with these minor interruptions in mental improvement there was a concomitant exaggeration of the parkinsonian symptoms. He continued, however, to make steady improvement. He spent a week-end at home, where he was happy and enthusiastic; he was discharged on March 26, 1936, as recovered. On discharge he showed only mild apprehensiveness, which his wife thought was no greater than he usually showed. Physically the parkinsonian symptoms were much in abeyance. He walked briskly, although with the body slightly bent, and showed almost normal facial expression. Associated movements were present to a slightly diminished degree. Cogwheel rigidity had disappeared, and there was no propulsion or retropulsion. (At present the arms are more flexed; he receives less scopolamine and is more apprehensive.)

The most interesting point illustrated in this case is the relationship between the mental and the physical symptoms. With the development of the parkinsonism his usual apprehensive and obsessional nature became exaggerated to a psychotic degree, only to recede concomitantly with the beneficial effects of therapy with scopolamine hydrobromide. Bromberg has pointed out that the postencephalitic paranoid-hallucinatory states are usually transient.

The possibility that the physical improvement may have been the direct result of the mental improvement must also be borne in mind, for every one is aware of the temporary changes which may be produced in parkinsonian symptoms by emotional stimuli. Nevertheless, I am inclined to believe that the physical symp-

toms produced interference with the usual automaticity of adjustment, which permitted a break along the lines of the patient's usual mental peculiarities. For financial and other reasons, it did not seem wise to make the desirable test of omitting treatment with scopolamine in order to observe the effect of the return of marked physical symptoms.

In a lengthy article (The Mental Pictures in Schizophrenia and in Epidemic Encephalitis, *Am. J. Psychiat.* **6**:413-465 [Jan.] 1927) in which he brought out similarities and variations in the mental states of schizophrenia and encephalitis, Jelliffe stated. "In no field of neuropsychiatry has a greater analytic opportunity been offered to explain the physiopathology of psychomotor manifestations than that which this overlapping or partial identification of behavioristic anomalies in encephalitis and schizophrenia shows itself." Nevertheless, knowledge of the localization of various psychic functions continues to be so meager that attempts to correlate the anatomic and physiologic characteristics of the lesions of encephalitis with the various psychotic manifestations are still extremely unsatisfactory.

DISCUSSION

DR. H. H. MERRITT: Have you tried benzedrine in either of these cases?

DR. W. N. HUGHES: In cases in which the disease starts early, for example, in that of the boy, do you think that the encephalitic process continues to progress and finally to account for the symptoms, or do you think that some new condition arises?

DR. J. B. MCKENNA: There are many reports in the literature of cases of schizophrenia following an attack of neurologically definite encephalitis. Jelliffe emphasized in his article the similarity of the picture of schizophrenia without known encephalitis to that of schizophrenia with known encephalitis. Many others have pointed out that there is considerable difference between schizophrenic reactions complicating parkinsonism and those not associated with disease. We have not used benzedrine. No drugs were given to the boy. I do not know personally whether the encephalitis was progressive in this case. I think that possibly there were symptoms which had passed unobserved by the physician since early childhood. As a fact, the mother pointed out that symptoms were present in early years, such as awkwardness with the hands and the like.

UNSTEADINESS OF THE HEART RATE IN PSYCHOTIC AND NEUROTIC STATES. DR. JOHN C. WHITEHORN and DR. HELEN RICHTER.

This article will be published in full in a later issue of the ARCHIVES.

Book Reviews

For Stutterers. By Smiley Blanton, M.D., and Margaret Gray Blanton, with Introduction by J. Ramsay Hunt. Cloth, $2. Pp. 191. New York: D. Appleton-Century Company, Inc., 1936.

The book is written from the standpoint of mental hygiene and is directed to the physician, parent and teacher and "those people with the symptom called stuttering." The book is without question one of the best treatises on the subject that has yet appeared, and whatever the future may bring to modify or add to the present status of the problem of stuttering, the main theories and facts which the Blantons present will doubtless stand as permanent contributions. The Blantons have been pioneers in this country in the study of the pathogenesis and treatment of stuttering, and their approach, unlike that of so many others interested in this problem, has been that of open-minded observation and critical analysis in many cases of patients of all ages over a period of years, taking into account and evaluating not one but all the possible factors that affect speech and result in stuttering. Years of observation and research have led the Blantons to the convicion that stuttering is merely a symptom—the expression of an abnormal psychic and emotional state, a neurosis that has taken root in early childhood as the result of inadequate emotional adjustment to the environment. Stuttering, then, is regarded as a conspicuous symptom of an anxiety neurosis. In each stutterer there is a particular cause for the neurosis, which expresses itself overtly in the "stutter." Treatment for stuttering is, therefore, directed primarily toward the cause of the neurosis. The essential factors in treatment are readjustment of environment, individual guidance and psychoanalysis, the age of the patient and a variety of circumstances determining where the main emphasis shall be placed. This concept of the etiology and the therapy of stuttering is now accepted not only by a small, though enlarging, group of psychiatrists, psychoanalysts and speech workers but by many mature and intelligent persons who have the symptom called a stutter.

The book starts with a short chapter addressed primarily to the stutterer, in which a sympathetic mutual understanding is established between the authors and the reader. In the second chapter there is a brief account of the essential factors in the development of normal speech which are vital to an understanding of the later discussion of the causes and treatment of stuttering. The development of "speech stages" is described: first, a process of stabilizing sounds selected for words and, second, the suppression of infantile and nonspeech movements during normal speech. Speech is not inherited: Speech is learned. The "parts of the body that are utilized by speech are only borrowed for speech and have their first and most vital use in some other field of activity," such as chewing, suckling, swallowing, vomiting and breathing, just as the primary use of the hand is for holding objects, though it is later used for writing, by training the various muscle groups for this highly intricate and artificial function of civilized life. The relation of the nervous system to the eventually unconscious, automatic control of speech, through the establishment of normal patterns of neuromuscular activity in speech, is described; then the rôle of the lower brain centers—the thalamus and the basal ganglia—and, finally, that of the cortex in relation to normal speech and stuttering are discussed. The physical symptom stuttering is attributed to "an emotion that blocks off [the] control of the cortex over the thalamus and lower nerve centers and allows the primitive patterns" (infantile oral activities) to assert themselves and supplant normal speech movements. It is important for the reader to bear this thesis in mind, both for an understanding of the Blantons' theories of the cause of stuttering and its treatment and as a criticism of other theories of stuttering, including that based on the experimental evidence of interference in cerebral dominance.

The third and fourth chapters deal with the "different levels of the mind" and the "conscience" and include a short description of the development and salient characteristics and functions of the conscious, the preconscious and the unconscious and of repression, censor and conscience. These chapters serve as a groundwork for an understanding of the next chapters, dealing with "anxiety" and "emotional patterns" in relation to the psychogenesis of stuttering, and to explain the basis for the emotional blocks which interfere with the control of the cortex over the lower brain centers, releasing the primitive or infantile oral patterns which result in stuttering. Then follows a chapter on "the family and emotional patterns," an analysis of the psychic patterns operating for happiness or for disharmony in the person's close environment and their potential effects on his psychic life.

Chapter IX is a description of the symptom stuttering and its bizarre variations and of the anxiety state, which will be of particular interest to the nonstutterer. It is estimated that 5 per cent of the male population and 1 per cent of the female have stuttered at one time or another.

Chapter XI is devoted to a concise exposition of the Blantons' beliefs regarding the cause of stuttering. To the reviewer it is the soundest conception yet presented. It takes into consideration the neurologic, temperamental, environmental, psychic and emotional components. On the basis of their observations and theories, the Blantons have developed a logical course of treatment, the essence of which is environmental and individual psychiatric readjustment, with psychoanalysis when it is indicated. Treatment is aimed at the anxiety neurosis which underlies the symptom—the stutter. In the chapters that follow—on treatment and on what the parent, the teacher, the stutterer and the public can do—and in the chapter entitled "What Chance of Recovery," much detail of treatment is given, frequently illustrated by extracts from case studies. Special emphasis is placed on the prevention of emotional aberrations and anxiety states in early childhood which may lead to stuttering and on the early recognition and treatment of stuttering. In the child particularly, treatment is a "community project, the community consisting of the person with the disability, the members of the family, the teachers and some one in charge who understands the problems of adjustment." The approach to the problem should be entirely one of readjustment of the child to its parents, playmates, routine and general environment. Retraining of speech should be omitted. In the adolescent and the adult patient treatment is more an individual and a personal matter, and here psychiatry and psychoanalysis play dominant rôles.

Child Psychiatry. By Leo Kanner, M.D. With prefaces by Adolf Meyer, M.D., and Edwards A. Park, M.D. Price, $6. Pp. 527. Springfield, Ill.: Charles C. Thomas, Publisher, 1935.

This is an excellent textbook that fills a real need. It is also an exposition of a new point of view, which is sane and appealing but perhaps overstressed, and at times a bit polemic. As a textbook it is better than anything that is at present available in the field. It is clear, concise and well arranged; it is comprehensive and in close touch with modern trends. If it is added that the style is fluent and terse, the bibliography copious and well selected and the grouping of the material ably conceived in terms of headings and subheadings, the qualities of the work as a textbook may almost be set down as an unbroken series of virtues. That in a textbook on child psychiatry the major psychoses should be relegated to the last descriptive chapter, just ahead of the appendix on "children's suicide" and that the topic should be assigned but 23 of a total of 527 pages is a logical sequence of the new point of view and may pass muster in view of the relative rarity of major psychoses in children.

The point of view expounded in the book is that of Adolf Meyer on psychobiology. It is presented with force and clarity, and the attempt to weave it into the fabric of a textbook is novel. The vital importance of the concept of total personality" is underlined; the terms "integration" and "synthesis" appear on prac-

tically every page. There is much stress on "objective observation" and on the necessity of working with "objective material." While the stress is undoubtedly justified, it is not supplemented with an outline of objective methods. One is referred to the revealing material to be gained from an expertly conducted interview, to the help offered by a well organized social service and to the diagnostic and therapeutic virtues of follow-up investigation. The emphasis is commendable and perhaps needed.

Nomenclature in psychiatry has always been a source of pointless argument. Kanner justly ridicules the labels "neurosis" and "neuropathic constitution," but what he offers in their place is of questionable applicability: "a reformulation of the complaint on the basis of the available data." Several sample "reformulations" are listed on page 115, for example: "Lifelong feeding problem and frequent diurnal complaint on the basis of the available data." Several sample "reformulations" family of four, badly spoiled by an invalid father and a hypochondriacal mother." Such brief summaries certainly present the situation better than a diagnosis such as neurosis or behavior problem but it is obvious that one must have both sorts of labels and that one supplements the other.

Kanner is at his best when he discusses cases and behavior trends. The chapters on antisocial trends, sexual difficulties and attack disorders are compact, with well chosen detail and apt analysis. Speech disorders are well discussed. In all these important sections the advice given as to treatment is sane and specific. Outworn creeds are frankly discarded, and it is pointed out that usually the child needs treatment in many social ways and that rarely does the symptom have to be treated. This is especially well brought out in respect to stuttering and masturbation. The discussion of the various forms of dementia praecox (parergastic reaction form) and of the manic-depressive disorders (thymergastic reaction form) differs in no particular from traditional kraepelinian presentation, except for a wise condensation of the material.

The book fills a real need; there is nothing like it in medical literature. By virtue of its many excellent features, it is bound to run through new editions; one might, therefore, suggest to the author that part of the historical matter is too wordy and that some of the polemic portions detract from the spirit of objectivity. Psychobiology has rendered a signal service to medicine in general and to psychiatry in particular by its wholesome emphasis on the concept of total personality, but it is in danger of marring its record by overemphasis. On the whole, the book is to be strongly recommended as a good exposition of a difficult subject which avoids the pitfalls of schools and hobbies, gives the facts well and tells how to help patients.